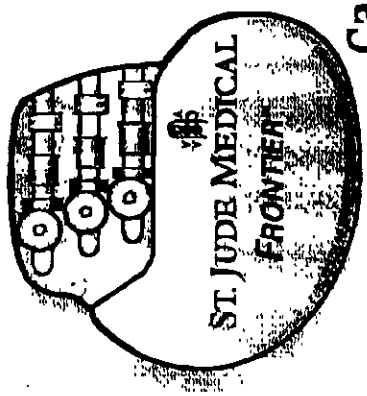
USER'S MANUAL

ST. JUDE MEDICAL

FRONTIER™
Model 5508L

Cardiac Resynchronization
Therapy Pacemaker (CRT-P)



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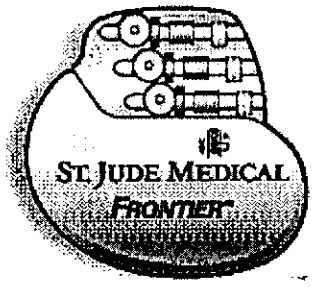

Figure 1. Frontier Model 5508L Cardiac Resynchronization Therapy Device

Description

The Frontier™ pulse generator is a multi-site, implantable cardiac resynchronization therapy pacemaker (CRT-P) with resynchronization therapy capabilities, intended for use with a St. Jude Medical® left heart pacing lead. The Frontier device is equipped with automatic rate-adjusting algorithms, patient safety features, and diagnostic tools and tests. The Frontier devices contains the Omnisense® accelerometer activity sensor to provide rate-modulated operation.

In addition, with the Frontier device, the Model 3510/3500 Programming System offers:

- On-screen Reference Manual
- Floppy disk database interface
- Continuous real-time printing of ECG, EGM, and Markers (only available on the Model 3510 Programmer)
- FastPath™ Summary and Measured Data Screens (only available on the Model 3510 Programmer)

A single setscrew for each lead secures the pin within the connector. The device header accepts unipolar or bipolar IS-1 and VS•1, or 3.2 mm leads.

Please refer to the physician User's Manual specific to the device being implanted.

Indications and Usage

Implantation of the Frontier™ Cardiac Resynchronization Therapy System is indicated for:

INDICATIONS AND USAGE

Implantation of the Frontier™ Cardiac Resynchronization Therapy System is indicated for:

1. Maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure.
2. The reduction of the symptoms of moderate to severe heart failure (NYHA Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy, and have a left ventricular ejection fraction ≤35% and a prolonged QRS duration.

CONTRAINDICATIONS

Implantation of the Frontier™ Cardiac Resynchronization Therapy System is contraindicated in patients who have been implanted with an implantable cardioverter-defibrillator (ICD).

For specific indications and contraindications associated with individual modes, refer to Operating Modes on page 42.

WARNINGS

To prevent permanent damage to the pulse generator and tissue damage at the electrode/tissue interface:

- ***Electrosurgery.*** Do not use electrosurgical devices in the vicinity of an implanted pulse generator. If electrocautery is necessary, use a bipolar cauterizer or place the indifferent electrode as far from the pulse generator as possible.
- ***Lithotripsy.*** Do not focus a lithotripsy beam within six inches of the pulse generator. Program the device to *Sensor* Off prior to lithotripsy to prevent inappropriate increases in the pacing rate. A thorough assessment of device's function with special attention to the sensor should be performed following exposure to lithotripsy.
- ***Therapeutic Radiation.*** Do not use ionizing radiation in the vicinity of an implanted pulse generator.

- **Therapeutic Radiation.** Do not use ionizing radiation in the vicinity of an implanted pulse generator. Radiation therapy may damage the electronic circuitry of the device.
- **Ultrasound Treatment.** Do not use therapeutic ultrasound within six inches of the pulse generator.
- **Ventricular Sensing.** Ventricular Sensitivity should be programmed to the highest setting (lowest sensitivity) that will provide ventricular sensing with adequate sensing margin. Left ventricular lead dislodgement, to a position near the atria, can result in atrial oversensing and ventricular inhibition.

Perform a thorough assessment of the pulse generator's function following exposure to any of the above.

Backup VVI Operation. In rare instances, the Frontier™ device may revert to Backup VVI operation at the programmed settings listed in Table 1. These values are not programmable.

When the device has reverted to Backup VVI operation, the programmer will display a pop-up message indicating that the device is operating at the Backup VVI values. Press [Continue] and follow the on-screen instructions.

Under most conditions, the previously programmed settings can be restored. The programmer will execute a short routine (approximately five minutes) to restore the previously programmed settings. When the routine is complete, a Device Status Report will be generated. This report should be returned to the St. Jude Medical location indicated on the report. Normal follow-up testing should be performed and the restored parameter settings should be reviewed.

Parameter	Value
Mode	VVI
Base Rate	67.5 ppm
Pulse Configuration	Unipolar
Sense Configuration	Unipolar Tip
Pulse Amplitude	4.0 V minimum
Pulse Width	0.6 ms
Refractory Period	320 ms
Sensitivity	2.0 mV

Table 1. Backup VVI Settings

Elective Replacement Indicator (ERI). At ERI, the nominal life of the Frontier device is three months. When the pulse generator exhibits signs of ERI, described on page 67, it should be replaced expeditiously.

Patient follow-up visits should be scheduled at an appropriate frequency so that ERI can be detected well before End-of-Life (EOL).

Precautions

- **For single use only.**

Sterilization

- Do not implant or resterilize a pulse generator that has been contaminated by contact with body fluids.
- Do not resterilize the device more than once.
- Do not implant a device from a damaged package without resterilizing it.

- To sterilize the pulse generator, use ethylene oxide gas at temperatures not exceeding 50° C (122° F), according to the sterilizer manufacturer's instructions. Allow proper aeration per local and national ordinances.[1]
- Do not sterilize the device with an autoclave, steam, gamma radiation, or ultrasonics.
- Resterilization of the Frontier™ device does not change the "use before" date established at the time of manufacture.

Storage and Handling

- **Mechanical Shock.** St. Jude Medical® devices are ruggedly constructed. However, if you suspect the device has been damaged, do not implant it; return it to St. Jude Medical.
- **Temperature.** Do not subject the device to temperatures above 50° C (122° F) or below –5° C (23° F). Exposure to temperatures below 0° C may cause false ERI indications. Following exposure to extreme temperatures, warm the device to room temperature. If ERI indications are still present, return the device to St. Jude Medical.
- **Incineration.** Do not incinerate the device.

Preparation for Implantation

- **Package Label.** Before opening the sterile package, carefully read the label and verify that the package contains the desired device.
- **Verifying Operation.** Before opening the sterile package, verify that the device is operating properly by interrogating it in the package. Remove the magnet and position the Model 3510/3500 Programmer telemetry wand over the package and select "Interrogate." Then, select the "Meas. Data/Diagnostics" tab. The unit's Measured Data should indicate normal voltage and battery status, and the programmed parameters should be identical to the Shipped Settings listed on the package label and in Table 22 on page 71.
- **Package Integrity.** Ensure that the package has not been opened or in any way compromised. If damage is suspected, return it to the manufacturer.
- **"Use Before" Date.** Do not implant the device after the "use before" date printed on the label.
- **Opening the Package.** If interrogation of the device in its sterile packaging indicates normal functioning, remove it from the package. The package's outer tray can be opened in nonsterile surroundings. However, when opening the inner tray, complete sterile technique must be observed (Figure 2).

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[1] See also AAMI GVR-1987, Good Hospital Practice: Ethylene Oxide Gas – Ventilation Recommendations and Safe Use.

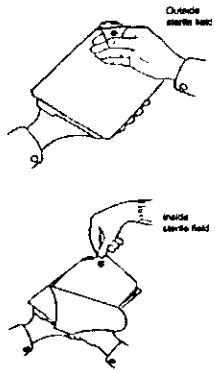

Figure 2. Opening the Sterile Package

Pre-Implant Testing

- **Compatible Leads.** In the Frontier™ device, use only a St. Jude Medical lead for the left ventricular lead, such as the Aescula™ left heart lead. The device's Quick Lock® header accepts unipolar or bipolar IS-1 and, VS•1, or 3.2 mm leads. Prior to implantation, make sure the leads fit easily and snugly into the pulse generator's header.
- **Leads Testing with Pacing System Analyzer.** After implanting the leads, capture and sensing thresholds should be determined with a pacing system analyzer (PSA) before implanting the device. Connect the negative (black) PSA terminal to the portion of the lead terminal pin corresponding to the tip electrode. The positive (red) terminal should be connected to the ring electrode portion of the lead pin for bipolar leads or to an indifferent electrode. For more information on conducting capture and sensing threshold tests, please consult the PSA technical manual.
- **PSA Adaptor Probes.** Use only IS-1 PSA cable adaptor probes when testing the pulse generator. Other probes may damage the connector.
- **Establishing Baseline Ventricular Capture/Sensing Thresholds.** After the leads have been implanted and before they are connected to the device, separately identify and document the baseline morphology for capture and sensing thresholds for each ventricular lead. Once the baselines are established, determine if the ECG or IEGM recordings can help discriminate biventricular capture, univentricular capture, and native depolarization for each lead. In a cardiac resynchronization therapy system. the ECG may display two distinct capture loss morphologies, because the left and right chambers often have different pacing thresholds. To ensure that the device is losing capture on both sides of the heart, allow the test to run until a marked change in morphology occurs, indicating capture loss on both sides.
- **Device Testing with PSA.** Before implantation of the device, the clinician may wish to test the device using a compatible PSA with calibrated sensitivity and output settings. When the probe is attached to the pulse generator's connector, the programmed parameters should be identical to the Shipped Settings listed on the package label and in Table 22 on page 71.

Implantation

- **Ventricular Leads with Polished Platinum Tip Electrodes.** Pairing the Model 1055K ventricular lead with a polished platinum tip electrode lead may create a source impedance mismatch that could adversely affect sensing. Therefore, in the use of these leads, evaluate adequate sensing performance at the time of implant.
- **Case Markings.** Examine the markings on the pulse generator case and verify proper ventricular connection. Ventricular leads can be inserted into either ventricular port.
- **Setscrew.** Exercise caution when turning the setscrew, which may be backed out of the connector if turned counter-clockwise for more than two rotations.

Programming

- **Programmer.** The Frontier™ cardiac resynchronization therapy device can be interrogated and programmed with the Model 3510/3500 Programmer with Model 3307 software or higher version. For a list of programmable parameters and their programmable values, see Table 23 on page 75.
- **Setting Lead Type.** When the user interrogates the device for the first time, the programmer will prompt the user to set the Lead Type. Because some parameters are determined by the Lead Type (for example, Pulse Configuration), the user should set this parameter to Bipolar/Unipolar when the device is implanted. See Ventricular Lead Selection on page 59.
- **Lead Impedance Values.** Signals to and from the two ventricular leads are joined in the device's connector to form a single ventricular channel. Consequently, lead impedance values displayed on the programmer's Measured Data screen will reflect this dual lead configuration and will likely be less than the value seen in a single lead system.
- **Ventricular Pulse Amplitude** should be set according to the higher capture threshold measurement of the left and right ventricular leads. Typically, capture thresholds are higher in the left ventricle. Ensure that the device is capturing in both left and right ventricles before setting Ventricular Pulse Amplitude.
- **Follow-up Capture Threshold Measurements.** Because both ventricular leads are joined in a single ventricular channel, the clinician may be able to determine when capture is occurring in both, one, or no chambers by noting changes in the ECG morphology during a ventricular capture threshold test. See the Frontier Reference Manual for more information.
- **Emergency VVI.** When programming the device to Emergency VVI settings, press the programmer's Emergency VVI button only once. Settings for Emergency VVI can be found in the Frontier Reference Manual or by selecting the HELP button on the Model 3510/3500 Programmer.
- **AOO(R), VOO(R), and DOO(R) Modes** are primarily intended for temporary diagnostic use. Long-term use may result in competitive pacing, inducing potentially dangerous arrhythmias.

- **ODO, OVO, and OAO Modes** are not recommended for patients who would be adversely affected by even a short cessation of device function.
- **Noninvasive EP Testing.** Atrial or ventricular tachycardia or fibrillation may occur during noninvasive EP testing. Therefore, (1) closely monitor the patient, and (2) have emergency equipment for cardioversion/defibrillation readily available while conducting EP testing.
- **High-Output Settings.** Programming high-output settings with a high Base Rate may shorten the time to ERI.
- **Runaway Protection.** Hardware circuitry in the Frontier device prevents it from stimulating at rates higher than 190 ppm (± 10 ppm).

Environmental and Medical Therapy Hazards

The Frontier™ device is equipped with special shielding and filters that significantly reduce the adverse effects of electromagnetic interference (EMI) on the operation of the device.

Patients should be directed to exercise reasonable caution in avoidance of strong electric or magnetic fields. If the pulse generator inhibits or reverts to asynchronous operation while in the presence of electromagnetic interference (EMI), the patient should move away from the EMI source or turn the source off.

Advise patients to seek medical guidance before entering environments that could adversely affect the operation of the device, including areas protected by a warning notice preventing entry by patients with pulse generators.

Medical Procedures and Environments

In general, patients implanted with the Frontier™ device should not be exposed to hospital equipment that produces high electromagnetic field strength signals, such as diathermy machines and electrosurgical units.

- **External Defibrillation.** The electronic circuitry in the pulse generator provides protection from defibrillation discharges. Nevertheless, do not place defibrillator paddles directly over the pulse generator or lead. Following defibrillation, ensure that the pacemaker is operating correctly.
- **Magnetic Resonance Imaging (MRI).** MRI for patients with implantable pulse generators has been contraindicated by MRI manufacturers. Clinicians should carefully weigh the decisions to use MRI with pacemaker patients. Additional safety concerns include:
    - Magnetic and RF fields produced by MRI may increase pacing rate, inhibit pacing, cause asynchronous pacing or result in pacing at random rates
    - MRI may result in changes in capture thresholds due to heating of pacing leads in any patient
    - MRI may irreversibly damage the pulse generator

    - Patients should be closely monitored during the MRI
    - Assess the pulse generator function before and after exposure to MRI.
- **Ionizing Radiation.** Therapeutic ionizing radiation (for example, used in linear accelerators and cobalt machines) can permanently damage the device's circuitry. The effect of ionizing radiation is cumulative; the potential for damage to the device is proportional to the patient's total radiation dosage. If the patient must be exposed to ionizing radiation, protect the device during the procedure with local radiation shielding. If tissue near the implant site must be irradiated, it may be necessary to move the device to another area. Before and after exposure to radiation, evaluate the device operation to identify any adverse consequences.
- **Transcutaneous Electrical Nerve Stimulation (TENS).** To reduce the possibility of interference with the device function, place the TENS electrodes close to one another and as far from the device as possible. Before allowing unrestricted use of TENS in a home or other setting, screen the patient in a monitored environment for possible interaction.
- **Therapeutic Diathermy.** Avoid diathermy, even if the device is programmed off, as it may damage tissue around the implanted electrodes or may permanently damage the pulse generator.
- **Electrosurgical Cautery** can induce ventricular arrhythmias and/or fibrillation or may cause asynchronous or inhibited device operation. If use of electrocautery is necessary, the current path and ground plate should be kept as far away from the device and leads as possible. A bipolar cauterizer may minimize these effects. Following electrocautery, conduct a thorough assessment of the device.

Patient Environment

- **High-Voltage** transmission lines and equipment, arc or resistance welders, induction furnaces, and similar equipment may generate substantial EMI fields that may interfere with device operation.
- **Communication Equipment,** such as microwave transmitters[2], linear power amplifiers, or high-power amateur transmitters may generate sufficient EMI to interfere with the operation of the pulse generator. Advise patients to move away from this equipment to resume normal pacemaker operation.
- **Home Appliances** that are in good working order and properly grounded do not usually produce enough EMI to interfere with device operation. Electric vibrators, razors, and handtools held directly over the pulse generator may disturb its operation.
- **Twiddler's Syndrome.** Caution patients against manipulating the implanted pulse generator since it may result in lead damage or lead displacement.
- **Patient Activities.** Any activities that involve repetitive impacts or jarring (such as horseback riding, jackhammer use, etc.) may increase the pacing rate when the device's Sensor is programmed On. Caution patients against such activity and program Sensor parameters with these activities in mind.

[2] Home appliance microwave ovens do not interfere with device operation.

- **Theft Detection Systems.** Theft detection systems, such as those often located at the entrances and exits of stores and public libraries may disturb the function of the device only if the patient pauses in the path of the beam.

Figure 3. No Pacer Symbol

- **No Pacer Symbol.** Caution patients implanted with this device to avoid areas marked with the NO PACER symbol.
- **Cellular Phones.** A St. Jude Medical-designed protective filter in the Frontier device prevents cellular phone-generated electromagnetic signals from interfering with the operation of the device.[3]

Type	Description
NADC (TDMA 50)	North American Digital Communications (Time Division Multiple Access 50 Hz)
US (TDMA 11)	Time Division Multiple Access 11 Hz
CDMA	Code Division Multiplex Access
PCS (GSM 1.9 GHz)	Personal Communication Systems (GSM 1.9 GHz)

Table 2. Digital Phones Standards Tested

Clinical tests performed by St. Jude Medical and five independent organizations[4] have documented that devices which incorporate this protective filter are not affected by any known analog cellular phone systems or any of the digital cellular phone technologies listed in Table 2. No special precautions are required for patients using the cellular phones listed above. Phone systems not listed in have not been tested and their interaction with the device cannot be guaranteed.

You or your patient may wish to contact Technical Support (page 81) to obtain more information on the interaction of certain cellular phones and this device.

[3] Carrillo R, Williams DB, Traad EA, Schor JS. Electromagnetic filters impeded adverse interference of pacemakers by digital cellular telephones. *JACC* 1996; 27(2A):15A Abstract 901-22.

[4] Center for Devices and Radiological Health, FDA, Rockville MD; Medical Devices Bureau of Health, Ottawa, Ontario, Canada; Mount Sinai Medical Center of Greater Miami, Miami Beach FL; Center for Study of Wireless Electromagnetic Compatibility, University of Oklahoma, Norman OK; Qualcomm, Inc., San Diego, CA.

Explantation

- Do not reuse explanted pulse generators and leads.
- Clean explanted equipment with +1% sodium hypochlorite, rinse with water, dry.
- Return the explanted device to the manufacturer.
- Explant the device before cremation of a deceased patient.
- Hex wrenches are available for disconnecting a previously implanted pulse generator from the indwelling leads. To obtain the wrenches, contact your local St. Jude Medical representative.

Adverse Events

The safety data presented in this section includes data from the Post AV Node Ablation Evaluation (PAVE) study which received approval under PMA P030035. Based on the results of the PAVE study, the biventricular pacing system is being legally marketed for "maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure". The identical CRT-P system as was approved in PAVE was under study with the Ventricular Resynchronization Therapy Randomized Trial (VecToR) (IDE G000229) with the goal to obtain additional labeling for heart failure. The PAVE safety data is therefore presented with the VecToR safety data for completeness.

The PAVE clinical study began on August 16, 2000. As of August 5, 2003, (PMA clinical report date) there were 361 attempted implants in the PAVE (Post-AV Node Ablation Evaluation) study from centers in the United States and Canada with average implant duration of 13.0 months (range: 0.1 - 35.7 months).

The VecToR (Ventricular Resynchronization Therapy Randomized Trial) clinical study using the identical Frontier™ system began on October 11, 2000. As of September 7, 2004, there were 144 attempted implants, of which 120 were successful, from centers in the United States and Canada with average implant duration of 22.7 months (range: 0.1 - 45.3 months).

Death information was gathered and classified by an independent mortality committee of three practicing physicians according to a published classification scheme. A summary of the death classification from the PAVE and the VecToR studies are shown on pages 3 and 5.

Observed Adverse Events

The PAVE and VecToR studies' cumulative implant duration for all enrolled patients was 7,948 months with a mean of 15.7 ± 12.2 months (range of 0.1 to 45.3 months). The cumulative duration for patients in the investigational group (all patients from PAVE and VecToR except the RV group in the PAVE study) was 6,393 months (532.8 years).

During the entire study period for both studies, 230 adverse events were reported for the investigational group including 80 complications and 150 observations. Tables 6 and 7 summarize the complications and Table 8 summarizes the observations that occurred during the studies. System-related complications and observations are based on patients with the investigational system only (PAVE, N = 254; VecToR, N = 144; Total, N = 398). Procedure-related complications are based on total number of attempted implants (PAVE, N = 255; VecToR, N = 144; Total, N = 399).

An Adverse Event is defined as an unfavorable clinical event, which impacts, or has the potential to impact, the health or safety of a clinical study participant caused by, or associated with, a study device or intervention. An adverse event is classified as a Complication when it results in an injury or an invasive intervention (for example, lead repositioning after lead dislodgement) that would not have occurred in the absence of the implanted device and/or system components. An Observation is defined as an adverse event that is not associated with injury to the patient or an invasive intervention, but which is associated with the system under investigation, or the programming thereof.

PAVE Study

Primary Cause	RV (N=106)	BV (N=146)	LV (N=53)	Roll-in (N=56)	Total (N=361)
Cardiac: Arrhythmic	1	1	1	0	**3**
Cardiac: Other	7	3	3	2	**15**
Cardiac: Unknown	0	1	0	0	**1**
Non-Cardiac	4	2	5	4	**15**
Unknown	6	5	3	2	**16**
Total	**18**	**12**	**12**	**8**	**50**[5]
% Death	**17.0**	**8.2**	**22.6**	**14.3**	**13.8**

Table 3. All Deaths Reported in the PAVE Study

[5] One additional patient was consented, but died prior to any study related procedure.

VecToR Study

A summary of the death classification through the first 6-months post-implant is shown in Table 4 below.

Primary Cause	ON (N=59)	OFF (N=47)	Roll-in (N=38)	Total (N=144)
Non Sudden Cardiac	1	0	2	3
Sudden Cardiac	0	1	0	1
Non Cardiac	0	0	1	1
Total	**1**	**1**	**3**	**5**
% Death	**1.7**	**2.1**	**7.9**	**3.5**

Table 4. Deaths as Randomized Through Six Months

Table 5 lists the additional 20 total deaths reported that occurred after 6 months post-implant. Since all patients received the identical system and cross-over was allowed after 6 months, data was not stratified by treatment assignment.

Primary Cause	Total (N=144)
Non Sudden Cardiac	**8**[6]
Sudden Cardiac	**3**
Non Cardiac	**4**
Unknown	**2**
Unknown Presumed Sudden	**2**
Unknown-Sudden	**1**
Total	**20**
% of Patients	**13.8%**

Table 5. All Deaths Reported for Vector Study Beyond Six Months Post-Implant

An Adverse Event is defined as an unfavorable clinical event, which impacts, or has the potential to impact, the health or safety of a clinical study participant caused by, or associated with, a study device or intervention. An adverse event is classified as a Complication when it results in an injury or an invasive intervention (for example, lead repositioning after lead dislodgement) that would not have occurred in the absence of the implanted device and/or system components. An Observation is defined as an adverse event that is not associated with injury to the patient or an invasive intervention, but which is associated with the system under investigation, or the programming thereof.

During the entire study period for both studies, 230 adverse events were reported for the investigational group including 80 complications and 150 observations. Tables 6 and 7 summarize the complications and Table 8 summarizes the observations that occurred during the studies. System-related complications and observations are based on patients

[6] One death was felt to be related to the procedure by the independent external mortality committee, but not attributed to any components of the investigational system.

with the investigational system only (PAVE, N = 254; VecToR, N = 144; Total, N = 398). Procedure-related complications are based on total number of attempted implants (PAVE, N = 255; VecToR, N = 144; Total, N = 399).

Events	No. of Events	No. of Patients	% of Patients	Events/Device Months[7]
LV Lead Related:	**36**	**34**	**8.5**	**0.0056**
Acute LV Lead Dislodgement	11	11	2.8	0.0017
High Implant Thresholds (LV Lead)	8	8	2	0.0013
Diaphragmatic Stimulation	7	7	1.8	0.0011
LV Lead Loss of Capture	5	5	1.3	0.0008
High Pacing Thresholds (LV Lead)	2	2	0.5	0.0003
Chronic LV Lead Dislodgement	1	1	0.3	0.0002
LV Lead Fracture	1	1	0.3	0.0002
Pectoral Stimulation	1	1	0.3	0.0002
RA/RV Lead Related:	**8**	**7**	**1.8**	**0.0013**
Acute RA/RV Lead Dislodgement	4	3	0.8	0.0006
Chronic RA Lead Dislodgement	1	1	0.3	0.0002
RV Perforation	1	1	0.3	0.0002
RV Insulation Failure	1	1	0.3	0.0002
Lead Fracture (RA Lead)	1	1	0.3	0.0002

[7] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups for PAVE and the ON, OFF and Roll-in groups for VecToR. The cumulative duration in months in these groups was 6,393 months.

System - Other:	**4**	**4**	**1**	**0.0006**
Inadequate Lead Connection	2	2	0.5	0.0003
Ventricular Tachycardia	1	1	0.3	0.0002
Erosion (Pocket Erosion)	1	1	0.3	0.0002
Total System-Related	**48**	**41**	**10.3**	**0.0075**

Table 6. System-Related Complications for Investigational Group[8, 9, 10]

Events	No. of Events	No. of Patients	% of Patients	Events/Device Months[11]
Procedure Related:	**32**	**30**	**7.5**	**0.005**
Coronary Sinus Dissection During Implant	13	13	3.3	0.002
Pneumothorax	4	4	1	0.0006
CS Perforation at Implant	3	3	0.8	0.0005
Pericardial Effusion	2	2	0.5	0.0003
Ventricular Tachycardia at Implant	2	2	0.5	0.0003
Tamponade	2	2	0.5	0.0003
Complete Heart Block at Implant	1	1	0.3	0.0002
Cardiopulmonary Arrest at Implant	1	1	0.3	0.0002

[8]Each patient may have more than one complication in more than one category.

[9]System-related complications based on total number of attempted implants (N = 398).

[10]The Investigational Group consists of all patients from the PAVE and VecToR studies except the RV group from the PAVE study.

[11] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups for PAVE and the ON, OFF and Roll-in groups fro VecToR. The cumulative duration in months in these groups was 6,393 months.

Non-Sudden Cardiac Death	1	1	0.3	0.0002
Pulmonary Edema Post Ablation	1	1	0.3	0.0002
LV Lead Dislodgment During Ablation	1	1	0.3	0.0002
Hemothorax	1	1	0.3	0.0002
Total System-Related and Procedure-Related Complications	**80**	**70**	**17.5**	**0.0125**

Table 7 Procedure-Related Complications for Investigational Group[12, 13, 14]

Events	No. of Events	No. of Patients	% of Patients	Events/Device Months [15]
Diaphragmatic Stimulation	35	29	7.3	0.0055
Pectoral Stimulation	19	17	4.3	0.003
High Pacing Threshold (LV Lead)	18	18	4.5	0.0028
High Implant Thresholds (LV Lead)	10	10	2.5	0.0016
Loss of Capture (LV Lead)	9	9	2.3	0.0014
Hematoma at Implant	8	8	2	0.0013

[12]Each patient may have more than one complication in more than one category.

[13]Procedure-related complications based on total number of attempted implants (N = 399).

[14]The Investigational Group consists of all patients from the PAVE and VecToR studies except the RV group from the PAVE study.

[15] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups for PAVE and the ON, OFF and Roll-in groups fro VecToR. The cumulative duration in months in these groups was 6,393 months.

CS Dissection	6	6	1.5	0.0009
Fatigue	6	6	1.5	0.0009
Infection	6	6	1.5	0.0009
Heart Failure - Worsening	3	3	0.8	0.0005
Telemetry Error	3	2	0.5	0.0005
Oversensing	3	3	0.8	0.0005
Discomfort - Device Site	2	2	0.5	0.0003
Thrombosis	2	2	0.5	0.0003
VVI Back-Up	2	2	0.5	0.0003
Stuck Stylet	2	2	0.5	0.0003
Undersensing (RA Lead)	1	1	0.3	0.0002
Loss of Capture-Intermittent (LV Lead)	1	1	0.3	0.0002
Hypotension	1	1	0.3	0.0002
Palpitation	1	1	0.3	0.0002
Arrhythmia - Torsades	1	1	0.3	0.0002
Noise on IEGM	1	1	0.3	0.0002
Dyspnea on Exertion	1	1	0.3	0.0002
RV Back-up Pacing Due to PVCs	1	1	0.3	0.0002
Acute LV Lead Dislodgment (minor)	1	1	0.3	0.0002
RV Loss of Capture	1	1	0.3	0.0002
LV Lead Undersensing	1	1	0.3	0.0002
Medication Reaction	1	1	0.3	0.0002
Pneumothorax	1	1	0.3	0.0002
CS Perforation	1	1	0.3	0.0002
Pre-Syncope	1	1	0.3	0.0002
Syncope	1	1	0.3	0.0002
Total Events	150	112	28.1	0.0235

Table 8. Observations for Investigational Group[16, 17, 18]

[16]Each patient may have more than one observation in more than one category.

Potential Adverse Events

Potential adverse events associated with the use of the transvenous leads and pacing systems include:

- Body rejection phenomena
- Cardiac/coronary sinus dissection
- Cardiac/coronary sinus perforation
- Cardiac tamponade
- Coronary sinus or cardiac vein thrombosis
- Death
- Device migration and pocket erosion
- Endocarditis
- Excessive bleeding
- Hematoma/seroma
- Induced atrial or ventricular arrhythmias
- Infection
- Local tissue reaction; formation of fibrotic tissue
- Loss of pacing and/or sensing due to dislodgment or mechanical malfunction of the pacing lead
- Myocardial irritability
- Myopotential sensing
- Pectoral/diaphragmatic/phrenic nerve stimulation
- Pericardial effusion
- Pericardial rub
- Pneumothorax/hemothorax
- Pulmonary edema
- Rise in threshold and exit block
- Thrombolytic or air embolism
- Valve damage

The following in addition to the above, are potential complications associated with the use of rate modulated pacing systems.

- Inappropriate, rapid pacing rates due to sensor failure or to the detection of signals other than patient activity.
- Loss of activity-response due to sensor failure.

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[17]Observations based on total number of attempted implants (N = 398).

[18]The Investigational Group consists of all patients from the PAVE and VecToR studies except the RV group from the PAVE study.

A coronary sinus venogram is unique to lead placement in the cardiac venous system, and carries risks, such as renal failure, cardiac or coronary sinus dissection, and cardiac or coronary sinus perforation.

Potential complications reported with direct subclavian venipuncture include hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage, and rarely death.

Summary of Clinical Investigations

PAVE Study

A prospective, randomized, controlled, multi-center clinical trial conducted at 49 participating sites (44 in the US, 5 in Canada) compared the safety and effectiveness results for patients receiving the Frontier™ Model 5508 pulse generator and the Aescula™ 1055K Left Heart Lead to those receiving legally marketed right ventricular pulse generators and standard leads following an AV nodal ablation for chronic atrial fibrillation. Chronic AF is defined as persisting without interruption for at least one month.

The study's cumulative implant duration for all enrolled patients was 4,684 months with a mean of 13.0 ± 9.6 months (range of 0.1 to 35.7 months). Two hundred and six patients underwent successful LV lead placement. The cumulative duration for all investigational patients (BV, LV and Roll-in groups only) was 3,129 months.

For this randomized study, the key inclusion criteria were:

- Patients who will undergo complete AV nodal ablation for chronic atrial fibrillation (defined as persisting without interruption for at least one month) resulting in complete AV block
- Patients who are on a stable medical therapy regimen, and
- Patients who are able to complete the six-minute walk with the only limiting factor(s) being fatigue and/or shortness of breath.

Key study exclusion criteria were:

- Patients who are classified as NYHA Class IV
- Patients who can walk > 450 meters in six-minute walk test
- Patients who have an implanted ICD or being considered for implant of an ICD
- Patients with prosthetic valve replacements
- Patients with severe musculoskeletal disorder(s). and
- Patients who cannot independently comprehend and complete the quality of life questionnaire.

The overall study population included 361 patients. One hundred and forty-six were randomized to BV, and 106 were randomized to RV. In addition, 53 were randomized to

LV pacing under a previous revision of the investigational plan. Fifty-six were "Roll-in" patients (nonrandomized) and received the biventricular pacing system (Frontier pulse generator and Aescula lead system). All patients had permanent pacemaker implant indication following an elective AV nodal ablation for chronic atrial fibrillation. The mean age was 69.2 ± 10.0 years; 34.3% were female and 65.7% were male. Fifteen percent of the patients had no diagnosis of heart failure or were NYHA Class I, 48% were NYHA Class II, and 37% were NYHA Class III prior to implant. Safety data from all patients were reported.

Primary Objectives and Results

1. Freedom from system-related complications through six months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from system-related complications for the BV group will not be less than 70%. A system-related complication was defined as a complication that is caused by a failed pacing system. A pacing system refers to all implanted components, including the pulse generator, leads, and the interaction of these components.

Results: There were 29 system-related complications in 26 patients within six months follow-up. The freedom from system-related complications is 87.8% with a lower bound of 84.0%. Objective met.

2. Freedom from pulse generator-related complications through six months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from pulse generator-related complications for the BV group through six months will not be less than 90%.

Results: There were no pulse generator-related complications through six months. The survival rate is 100% with a lower bound of 98.6%. Objective met.

3. Freedom from Aescula™ lead-related complications through six months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula™ lead-related complication for the BV group through six months will not be less than 75%.

Results: There were 25 Aescula lead-related complications in 24 patients through six months follow-up. The freedom from Aescula lead-related complications is 88.2% with a lower bound of 84.4%. Objective met.

4. Rate of successful implantation of the Aescula™ lead

Objective: The lower bound of the one-sided 95% confidence interval of the successful implantation rate of the Aescula lead for the BV group will not be less than 80%. The

success rate was defined as the proportion of patients who received the complete pacing system.

Results: One hundred and forty-six patients randomized to BV underwent attempted implants. One hundred and twenty-five were successfully implanted. The rate of successful implant of the Aescula lead for BV group is 86% with a lower bound of 81%. Objective met.

5. Aescula™ lead pacing threshold at six months

Objective: The upper bound of the one-sided 95% confidence interval of mean capture threshold will not be greater than 3.0 V for the BV group at six months.

Results: The pacing threshold at six months for the BV group is 2.27 V ± 1.66 V with an upper bound of 2.53 V. Objective met.

6. Exercise capacity as measured by distanced walked in six-minute walk test

Objective: To determine if the treatment group (BV) shows a statistically significant improvement over the control group (RV) at the six months follow-up time.

Results: The treatment group (BV) showed statistically significant improvement over the control group (RV) in distance walked from pre-implant to six months ($p = 0.03$). The BV group also had a greater percentage of patients showing improvements than the RV group ($p = 0.035$). Figure 4 illustrates the improvement in the six-minute walk between BV and RV groups. Table 9 outlines the improvement distribution in the six-minute walk between BV and RV groups.

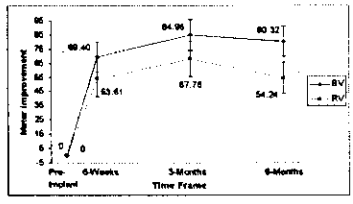

Figure 4. Improvements in Six-Minute Walk Distance in BV and RV Groups (p = 0.03)

	RV (N = 66)	BV (N = 84)
Improved (> 5 m)	46 (69.70%)	69 (82.14%)
No Change (–5 to 5 m)	4 (6.06%)	4 (4.76%)
Worsened (< –5 m)	16 (24.24%)	11 (13.10%)

Table 9. Distribution of Improvement in BV and RV Group in Six- Minute Walk (p = 0.035)

Secondary Objectives and Results

1. Quality of life as measured by SF-36 score

Objective: To determine if the BV group shows improvement over the RV group at the six-month follow-up in the health-related quality of life as measured by the SF-36 score.

Results: Using the SF-36 Quality-of-Life questionnaire, a standardized measurement of quality of life, the study found that for the six-week to six-month visit time period, the improvement in SF-36 scales was not different between groups.

2. Functional capacity as measured by peak VO_2

Objective: To determine if the BV group shows improvement in functional capacity, as measured by peak VO_2, from the six-week follow-up to the six-month follow-up.

Results: The BV group showed an improvement of 0.86 ml/kg/min in peak VO_2 from six weeks to six months measured during CPX testing ($p = 0.03$). The BV group also had a greater percentage of patients showing improvement in peak VO_2 ($p = 0.02$). Figure 5 illustrates the improvement in peak VO_2 in BV and RV groups. Table 10 outlines the distribution of improvement in peak VO_2 between BV and RV groups.

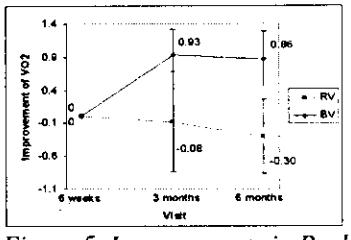

Figure 5. Improvements in Peak VO_2 in BV and RV Groups ($p = 0.03$ Within BV Group)

Change in Peak VO_2 (ml/kg/min)	RV (N = 10)	BV (N = 35)
Improved (> 0.5)	4 (40%)	21 (60.0%)
No Change (–0.5 to 0.5)	0 (0%)	4 (11.4%)
Worsened (< –0.5)	6 (60%)	10 (28.6%)
p-Value Within Group	0.38	0.02

Table 10. Distribution of Improvements in VO_2 in BV and RV groups

VecToR Study

The VecToR CRT-P study was designed to pursue approval for cardiac resynchronization therapy for a Heart Failure (HF) patient population, which, in the investigators' opinion, does not need the additional benefit of back up defibrillation. An identical system (i.e., Frontier biventricular pacing system) as used in the PAVE population was used in the

VecToR CRT-P population. The safety data presented shows that the system is safe for its intended use and demonstrates the safety of the Frontier CRT-P system.

The VecToR (CRT-P) study did not enroll sufficient numbers of randomized patients to meet its effectiveness objectives. Although the VecToR (CRT-P) study and the RHYTHM (CRT-D) study used different pulse generators (Frontier and Epic HF, respectively), both used the same biventricular pacing function which is delivered through the legally marketed SJM Aescula lead to provide cardiac resynchronization therapy. Data from the RHYTHM Study is used to demonstrate CRT effectiveness, as the patient populations in RHYTHM and VecToR are comparable.

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The VecToR study was a prospective, double-blind, randomized, controlled, multi-center clinical trial of patients with New York Heart Association Class III/IV congestive heart failure, and was conducted at 41 participating sites (39 in the US, 2 in Canada). The study compared the safety and effectiveness of cardiac resynchronization pacing therapy (CRT-P), using the Frontier Model 5508 pulse generator and the Aescula 1055K Left Heart Lead to no CRT-P therapy.

Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

1. Symptomatic ischemic or nonischemic dilated cardiomyopathy, which is not due to reversible causes.
2. Left ventricular end-diastolic diameter >54mm as measured by echocardiography.
3. Left ventricular ejection fraction ≤ 35% as measured by echocardiography.
4. QRS duration of ≥ 140 ms.
5. Stable but advanced heart failure due to left ventricular dysfunction (diagnosed for at least 6 months) despite stable conventional medical therapy.
6. Completed the 6-minute walk test as outlined in the protocol with the only limiting factor(s) being fatigue and/or shortness of breath.
7. Adequate cardiographic acoustic windows.
8. Provided informed consent for study participation and, are willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Exclusion Criteria

1. Can walk >450 meters during the 6-minute walk test.
2. Have standard bradycardia indications or likely to need pacing within the next 6-months.
3. Are classified as NYHA Class I or II.
4. Have a history of persistent or chronic atrial fibrillation or a history of atrial fibrillation which required intervention to revert to normal sinus rhythm.
5. Have an implanted cardioverter defibrillator (ICD) or, are being considered for implantation of an ICD.
6. Are contraindicated for an emergency thoracotomy.

7. Are considered status 1 for cardiac transplantation and are likely to receive transplantation within 1 year
8. Are being treated with parenteral inotropic agents (e.g., dobutamine) or have been treated with such agents within the past 30 days.
9. Have prosthetic valve replacement(s).
10. Have severe musculoskeletal disorder(s).
11. Are under the age of 18 years.
12. Are pregnant or plan a pregnancy in the next 6 months.
13. Are currently participating or participated within the past 30 days in any clinical investigation.
14. Have a life expectancy of less than 6 months.
15. Cannot independently comprehend and complete the Minnesota Living With Heart Failure questionnaire.
16. Are allergic to dexamethasone sodium phosphate (DSP).

To gain initial experience, investigators were given the option of prospectively determining that the first two patients implanted would not be randomized and would not count toward the implant success rate. However, these "Roll-In" patients met all inclusion criteria, were blinded to their treatment arm, and were followed per protocol. As such and as defined in the protocol, this "Roll-In" group is included in the safety analysis. All patients received the pacing system comprised of the investigational Frontier pulse generator and Aescula left heart lead, and a legally marketed right atrial and right ventricular lead. Patients were followed every 3 months for the first twelve months, and every six months thereafter. Patients in the CRT OFF group were allowed to cross over after completing the requirements of the 6-month visit.

As of September 7, 2004, the total time of follow-up from the time of successful implant in 120 patients was 2383 patient months. The average time of follow-up was 19.9 ± 8.9 (range 0.8 to 35.4) patient months.

Patient Population

The overall VecToR study population included 144 patients. Fifty-nine (59) patients were randomized to ON, and 47 patients were randomized to OFF. Revision C of the VecToR protocol excluded NYHA Class II patients. Thirty-eight (38) were "roll-in" patients (non-randomized) and received the cardiac resynchronization pacing therapy system (Frontier pulse generator and Aescula lead system). Safety analyses include all patients with the Frontier pulse generator and the Aescula left heart lead, including ON, OFF, and roll-in. The mean age was 67.1 ± 9.7 years and there were 62.5% male and 37.5% female. Twenty-nine percent (29%) of the patients were NYHA Class II, 65% were NYHA Class III, and 6% were NYHA Class IV prior to implant.

Primary Safety Objectives and Results

The primary safety objectives for the VecToR study are presented below.

1. FREEDOM FROM SYSTEM-RELATED COMPLICATIONS THROUGH SIX MONTHS

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from system-related complications will not be less than 70%. A system-related complication was defined as a complication that is caused by a failed pacing system. A pacing system refers to all implanted components, including the pulse generator, leads, and the interaction of these components.

Results: There were 12 system-related complications in 11 patients within six-months follow-up. The freedom from system-related complications is 90.7% with a lower bound of 86.4%. Objective met.

2. FREEDOM FROM PULSE GENERATOR-RELATED COMPLICATIONS THROUGH SIX MONTHS

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from pulse generator-related complications for the combined group through six months will not be less than 90%.

Results: There were no pulse generator-related complications through six months. The survival rate is 100% with a lower bound of 97.1%. Objective met.

3. FREEDOM FROM AESCULA™ LEAD-RELATED COMPLICATIONS THROUGH SIX MONTHS

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula™ lead-related complication through six months will not be less than 75%.

Results: There were 8 Aescula lead-related complications in 8 patients through six-months follow-up. All patients from the VecToR study who were successfully implanted are included in this analysis. The freedom from Aescula lead-related complications is 93.3% with a lower bound of 89.5%. Objective met.

4. RATE OF SUCCESSFUL IMPLANTATION OF THE AESCULA™ LEAD

Objective: The lower bound of the one-sided 95% confidence interval of the successful implantation rate of the Aescula lead will not be less than 80%. The success rate was defined as the proportion of patients who received the complete pacing system.

Results: A total of 144 patients who were randomized to CRT ON or OFF in the VecToR study and underwent attempted BV implants. One hundred and twenty (120) were successfully implanted. The rate of successful implant of the Aescula lead is 84% with a lower bound of 78% which does not meet the protocol defined objective for this endpoint (lower 95% confidence bound of 80%).

Deleted: The VecToR implants were performed in the early stage of the CRT technology, and consequently the LV lead implant success rate increased greatly in the recent study of PAVE and RHYTHM (86% and 87%, respectively) after experience was gained.

5. AESCULA™ LEAD PACING THRESHOLD AT SIX MONTHS

Objective: The upper bound of the one-sided 95% confidence interval of mean capture threshold will not be greater than 3.0 V for the combined group at six months.

Results: The electrical performance data of the LV lead were available on a total of 110 patients at six months. The pacing threshold at six months for the LV lead is 2.10 V with an upper bound 95% confidence interval of 2.34 V. Objective met.

RHYTHM Study

The RHYTHM ICD Study demonstrated that the SJM CRT-D system (Epic HF and Aescula lead) was safe and effective in NYHA Class III and IV heart failure patients with prolonged QRS duration and served as the basis for the recent PMA approved (PMA # P030054). The RHYTHM ICD study enrolled patients who also had a current ICD indication, which at the time the study was initiated included patients who were indicated for an ICD solely for primary prevention or prophylaxis (i.e., the patients were at risk of ventricular tachyarrhythmias and sudden death due to other clinical characteristics, but had not experienced a spontaneous or induced tachycardia).

The RHYTHM ICD study was a prospective, multicenter, randomized, double-blind, controlled clinical investigation designed to assess the safety and effectiveness of the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Classification of III or IV and a prolonged QRS duration. The objective of this clinical study was to verify the safety and effectiveness of the Epic HF ICD (Model V-338) system in an ICD indicated patient population with advanced heart failure (NYHA Classification III or IV) and prolonged QRS duration.

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Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

1. Approved indication for implantation of an ICD for treatment of a life-threatening ventricular tachyarrhythmia(s).
2. Symptomatic, advanced heart failure (ischemic or non-ischemic) not due to reversible causes, diagnosed for at least 6-months.
3. New York Heart Association (NYHA) Classification of III or IV, despite receiving a minimum of 90 days of appropriate pharmacological therapy.

4. Receive optimal pharmacological therapy for CHF (including angiotensin converting enzyme inhibitor and beta blocker, as tolerated) which has been stable during the 30 days prior to enrollment.
5. Left ventricular ejection fraction (LVEF) ≤ 35%.
6. Ventricular conduction delay manifested as a QRS duration ≥ 150 msec.
7. Ability to complete cardiopulmonary exercise stress testing and 6-Minute hall walk test, with the only limiting factor(s) being fatigue and/or shortness of breath.
8. Ability to independently comprehend and complete a quality of life questionnaire (Minnesota Living with Heart Failure).
9. Ability to provide informed consent for study participation and be willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Exclusion Criteria

1. Standard bradycardic indication for pacing.
2. History of chronic atrial fibrillation (continuous AF lasting > 1 Month) within 1 year prior to enrollment or have undergone cardioversion for AF in the past month.
3. Ability to walk > 450 meters during the 6-Minute walk test.
4. NYHA Classification of I or II.
5. Contraindication for an emergency thoracotomy.
6. Classification of Status 1 for cardiac transplantation or consideration for transplantation over the next 6-months.
7. Recent myocardial infarction, unstable angina or cardiac revascularization (PTCA or CABG) within 1 month of enrollment.
8. Recent CVA or TIA - within 3 months of enrollment.
9. Severe musculoskeletal disorder(s).
10. Pregnant or a planning for pregnancy in next 6-months.
11. Currently participating in, or has participated in any clinical investigation within the last 30 days. (the only exception being that of a registry trial)
12. Life expectancy of less than 6-months.
13. Less than 18 years of age.

All patients who met enrollment criteria underwent implantation of the Epic HF ICD system and a St. Jude Medical left ventricular pacing lead. ICD therapy was activated at the time of implant for all patients. Patients underwent Baseline evaluation between two weeks and 30 days following successful device implantation. Baseline was considered time zero for the purposes of evaluation of resynchronization study endpoints.

Patients were randomized following completion of Baseline testing and were assigned to either the treatment group (CRT ON) or the control group (CRT OFF) at a 2:1 ration. Patients who underwent unsuccessful implantation of the Epic HF ICD system were followed for a period of 30 days prior to withdrawal from the study. All patients who were successfully implanted were followed at 1, 3, 6 and every 3 months thereafter until the study was completed. Cross-over from the control group was allowed after completing the 6-month visit.

As of March 17, 2004, the total time of follow-up from the time of successful implant was 2205 patient months. The average time of follow-up was 12.1 ± 3.4 (range 0.3 to 20.3) patient months.

Patient Population

Of the 205 patients enrolled in the RHYTHM ICD study, one hundred and eighty-three (183) lead implant attempts were successful (180 successful on the first attempt and 3 successful on the second attempt). One additional patient had a successful left ventricular lead implant, but had high defibrillation thresholds. This patient was withdrawn from the study and received a heart transplant, leaving a total of 182 successful system implants.

Patients who were successfully implanted with the Epic HF ICD system had a Baseline visit approximately two weeks after implant, during which the following tests/assessments were performed: Electrical measurements on RA, RV and LV leads, cardiopulmonary exercise (CPET) test, echocardiogram, NYHA class assessment, 6 minute walk test, and Minnesota Living with Heart Failure questionnaire. Of the 182 patients with successful implants, two patients expired and one patient withdrew from the study before the Baseline visit and therefore, 179 patients had a Baseline visit. One additional patient who had a Baseline follow-up visit refused randomization and all the Baseline evaluations except device interrogation and electrical measurements, but remained in the study. Therefore, a total of 178 patients completed the requirements of the Baseline visit.

Primary Effectiveness Objective and Results

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CARDIAC RESYNCHRONIZATION THERAPY EFFECTIVENESS (PEAK VO_2)

Deleted: EFFICACY

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: In the intention-to-treat analysis, patients who crossed over from the CRT OFF group to the CRT ON group during the study were analyzed according to the original treatment group they belonged to. Table 11 contains a summary of the improvement in peak VO_2 values in the two treatment groups for this analysis. The average improvement in the CRT ON group over the CRT OFF group was approximately 1.9 ml/kg/min. The p-value was 0.001. Objective met.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	12.8 ± 3.7	11.2 ± 3.0
6-months	11.4 ± 5.6	11.7 ± 3.2
Change	-1.41 ± 4.6	0.52 ± 2.5
Overall improvement in CRT ON vs. CRT OFF = 1.9 ml/Kg/min		

Table 11. Improvement in Peak VO_2 Values (ml/kg/min) Intention-to-Treat Analysis (N=126)

Secondary Objective and Results

1. IMPROVEMENT IN NYHA CLASS AT 6-MONTHS OVER BASELINE

Objective: To determine if the treatment group (CRT ON) shows an improvement over the control group (CRT OFF) at six months.

Deleted: a statistically significant

Results: Table 12 shows the average change in NYHA Class from Baseline to 6-months for each group. Objective met.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	2.86 ± 0.52	3.01 ± 0.33
6-months	2.58 ± 0.73	2.53 ± 0.69
Change	-0.28 ± 0.63	-0.48 ± 0.65

Table 12. Baseline and Six Month NYHA Class (N=126)

2. IMPROVEMENT IN QUALITY OF LIFE AT 6-MONTHS OVER BASELINE

Objective: To determine if the treatment group (CRT ON) shows an improvement over the control group (CRT OFF) at six months.

Deleted: a statistically significant

Results: Patient quality of life (QOL) was assessed with the Minnesota Living with Heart Failure questionnaire. A lower score indicates an improvement in quality of life. Table 13 contains a summary of the improvement in Quality of Life in the two groups from baseline to 6 months.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± S (N = 83)
Baseline	42.0 ± 23	48.3 ± 24
6-months	45.4 ± 31	40.4 ± 22
Change	3.4 ± 31	-7.8 ± 22

Table 13. Improvement in Quality of Life Score (N=126)

The average improvement in the CRT ON group over the CRT OFF group was approximately 11 points. Objective met.

3. IMPROVEMENT IN SIX-MINUTE HALL WALK AT 6-MONTHS OVER BASELINE

Objective: To determine if the treatment group (CRT ON) shows an improvement over the control group (CRT OFF) at six months.

Deleted: a statistically significant

Results: Table 14 contains a summary of the improvement in 6-minute walk distance between baseline and 6 months.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	298 ± 94	284 ± 105
6-months	283 ± 150	297 ± 122
Change	-15 ± 142	13 ± 74

Table 14. Improvement in Six Minute Walk Distance (meters) (N=126)

The average improvement in the CRT ON group over the CRT OFF group was approximately 28 meters.

Additional Data

1. BIVENTRICULAR PACING AT 6-MONTHS

The average percentage of biventricular pacing at the 6-month visit in the 83 patients who were in the CRT ON group among the 126 patients in the primary resynchronization cohort was 95% ± 6%, with a range of 70% to 100%.

2. ECHO DATA

Echocardiographic analysis was performed at the baseline and 6-month follow-up visits. The following parameters were evaluated from the echocardiographic analysis: LVEDD, LVESD, LVEF, MR, E/A Wave Point Ratio, and Sphericity Index. Cardiac dyssynchrony (including Pre-Ejection Delay Time and Intraventricular Mechanical Delay) was also evaluated at baseline and 6-Months. Table 15 displays summaries of the improvement in these parameters between baseline and 6-months.

Parameter	CRT OFF (N = 40) Mean ± SD	CRT ON (N = 82) Mean ± SD
LVEDD (mm)	-2.4 ± 6.5	-4.3 ± 5.4
LVESD (mm)	-3.0 ± 6.4	-4.6 ± 7.0
LVEDV (ml)	-37 ± 53	-43 ± 69
LVESV (ml)	-36 ± 47	-43 ± 58
LVEF (%)	2.9 ± 6.2	4.3 ± 9.9
MR (grade)	0.10 ± 0.50	-0.06 ± 0.74
E/A Wave Point Ratio	-0.02 ± 1.2	-0.08 ± 0.8
Sphericity Index	0.02 ± 0.1	-0.02 ± 0.1
Pre-Ejection time (ms)	7.3 ± 33	-1.5 ± 52
IVMD (ms)	-6.4 ± 48	-14.5 ± 52
Tei Index	-0.05 ± 0.5	-0.4 ± 0.8
Contraction Interval (ms)	-55 ± 103	-94 ± 124

Table 15. Improvement in Echocardiography Parameters

USER'S MANUAL

ST. JUDE MEDICAL

FRONTIER™ II
Model 5586

Cardiac Resynchronization Therapy Pacemaker (CRT-P)

Frontier II Model 5586
Cardiac Resynchronization Therapy Pacemaker (CRT-P)
User's Manual

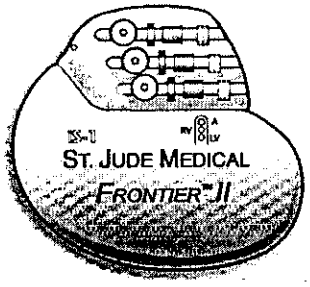

Figure 1. Frontier II Model 5586 Cardiac Resynchronization Therapy Device

Description

The Frontier™ II pulse generator is a multi-site, implantable cardiac resynchronization therapy pacemaker (CRT-P) with resynchronization therapy capabilities, intended for use with a St. Jude Medical® left heart pacing lead. Additionally, the Frontier™ II pulse generator allows independently programmable left and right ventricular outputs.

The Frontier II device is equipped with automatic rate-adjusting algorithms, patient safety features, and diagnostic tools and tests. The Frontier II device contains the Omnisense® accelerometer activity sensor to provide rate-modulated operation.

In addition, with the Frontier II device, the Model 3510 Programming System offers:

- On-screen Reference Manual
- Floppy disk database interface
- Continuous real-time printing of ECG, EGM, and Markers (only available on the Model 3510 Programmer)
- FastPath™ Summary and Measured Data Screens

A single setscrew for each lead secures the pin within the connector. The device header accepts unipolar or bipolar IS-1 short terminal pin leads.

The Frontier II device can be programmed with the Model 3510 programming system with Model 3307, v4.8M or higher programmer software. For detailed information on programming, testing and displaying diagnostic data, refer to the Frontier Reference Manual or select the HELP button on the 3510 programmer.

Please refer to the physician User's Manual specific to the device being implanted.

Please refer to the physician User's Manual specific to the device being implanted.

Indications and Usage

Implantation of the Frontier™ II Cardiac Resynchronization Therapy System is indicated for:

- Maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure.
- The reduction of the symptoms of moderate to severe heart failure (NYHA Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy, and have a left ventricular ejection fraction ≤35% and a prolonged QRS duration.

Contraindications

Implantation of the Frontier™ II Cardiac Resynchronization Therapy System is contraindicated in patients who have been implanted with an implantable cardioverter-defibrillator (ICD).

For specific indications and contraindications associated with individual modes, refer to Operating Modes on page 44.

Warnings

To prevent permanent damage to the device and tissue damage at the electrode/tissue interface:

- *Electrosurgery.* Do not use electrosurgical devices in the vicinity of an implanted device. If electrocautery is necessary, use a bipolar cauterizer or place the indifferent electrode as far from the device as possible.
- *Lithotripsy.* Do not focus a lithotripsy beam within six inches of the device. Program the device to *Sensor* Off prior to lithotripsy to prevent inappropriate increases in pacing rate. A thorough assessment of device function with special attention to the sensor should be performed following exposure to lithotripsy.

- **Therapeutic Radiation.** Do not use ionizing radiation in the vicinity of an implanted device. Radiation therapy may damage the electronic circuitry of the device.
- **Ultrasound Treatment.** Do not use therapeutic ultrasound within six inches of the device.
- **Ventricular Sensing.** Ventricular Sensitivity should be programmed to the highest setting (lowest sensitivity) that will provide ventricular sensing with adequate sensing margin. Left ventricular lead dislodgement, to a position near the atria, can result in atrial oversensing and ventricular inhibition.

Perform a thorough assessment of device function following exposure to any of the above.

Backup VVI Operation. In rare instances, the device may revert to Backup VVI operation at the programmed settings listed in Table 1. These values are not programmable.

Parameter	Value
Mode	VVI
Base Rate	67.5 ppm
Ventricular Pacing Chamber	RV Only
RV Pacing Configuration	RV Unipolar
Sense Configuration	RV Unipolar Tip
Pulse Amplitude	5.0 V
Pulse Width	0.6 ms
Refractory Period	335 ms
Sensitivity	2.0 mV

Table 1. Backup VVI Settings

Note: An RV lead must be used with the Frontier II device. Back-Up VVI pacing is delivered to the right ventricle only.

When the device has reverted to Backup VVI operation, the programmer will display a pop-up message indicating that the device is operating at the Backup VVI values. Press [Continue] and follow the on-screen instructions.

Under most conditions, the previously programmed settings can be restored. The programmer will execute a short routine (approximately five minutes) to restore the previously programmed settings. When the routine is complete, a Device Status Report will be generated. This report should be returned to the St. Jude Medical location indicated on the report. Normal follow-up testing should be performed and the restored parameter settings should be reviewed.

Elective Replacement Indicator (ERI). At ERI, the nominal life of the device is three months. When the device exhibits signs of ERI, described on page 67, it should be replaced expeditiously.

Patient follow-up visits should be scheduled at an appropriate frequency so that ERI can be detected well before End-of-Life (EOL).

Precautions

- For single use only.

Sterilization

- Do not implant or resterilize a device that has been contaminated by contact with body fluids.
- Do not resterilize the device more than once.
- Do not implant a device from a damaged package without resterilizing it.
- To sterilize the device, use ethylene oxide gas at temperatures not exceeding 50° C (122° F), according to the sterilizer manufacturer's instructions. Allow proper aeration per local and national ordinances.[1]
- Do not sterilize the device with an autoclave, steam, gamma radiation, or ultrasonics.
- Resterilization of a device does not change the "use before" date established at the time of manufacture.

Storage and Handling

- **Mechanical Shock.** St. Jude Medical® devices are ruggedly constructed. However, if you suspect the device has been damaged, do not implant it; return it to St. Jude Medical.
- **Temperature.** Do not subject the device to temperatures above 50° C (122° F) or below –5° C (23° F). Exposure to temperatures below 0° C may cause false ERI indications. Following exposure to extreme temperatures, warm the device to room temperature. If ERI indications are still present, return the device to St. Jude Medical.
- **Incineration.** Do not incinerate the device.

Preparation for Implantation

- **Package Label.** Before opening the sterile package, carefully read the label and verify that the package contains the desired device.
- **Verifying Operation.** Before opening the sterile package, verify that the device is operating properly by interrogating it in the package. Remove the magnet and position the Model 3510 programmer telemetry wand over the package and select "Interrogate." Then, select the "Meas. Data/Diagnostics" tab. The unit's Measured Data should indicate normal voltage and battery status, and the programmed parameters should be identical to the Shipped Settings listed on the package label and in Table 21 on page 71.
- **Package Integrity.** Ensure that the package has not been opened or in any way compromised. If damage is suspected, return it to the manufacturer.
- **"Use Before" Date.** Do not implant the device after the "use before" date printed on the label.
- **Opening the Package.** If interrogation of the device in its sterile packaging indicates normal functioning, remove it from the package. The package's outer

[1] See also AAMI GVR-1987, Good Hospital Practice: Ethylene Oxide Gas – Ventilation Recommendations and Safe Use.

tray can be opened in nonsterile surroundings. However, when opening the inner tray, complete sterile technique must be observed (Figure 2).

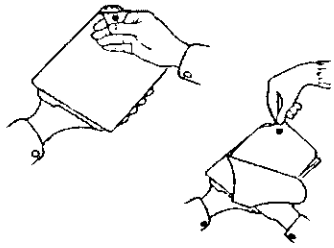

Figure 2. Opening the Sterile Package

Pre-Implant Testing

- **Compatible Pacing Leads.** Use only St. Jude Medical leads as the left ventricular lead in the Frontier™ II device. The device header accepts all unipolar or bipolar IS-1 short terminal pin leads. Prior to implantation, make sure the leads fit easily and snugly into the device's header.
- **Leads Testing with Pacing System Analyzer.** After implanting the leads, capture and sensing thresholds should be determined with a pacing system analyzer (PSA) before implanting the device. Connect the negative PSA terminal to the portion of the lead terminal pin corresponding to the tip electrode. The positive terminal should be connected to the ring electrode portion of the lead pin for bipolar leads or to an indifferent electrode. For more information on conducting capture and sensing threshold tests, consult the PSA technical manual.
- **PSA Adapter Probes.** Use only IS-1 PSA cable adapter probes when testing the pulse generator. Other probes may damage the connector.
- **Establishing Baseline Ventricular Capture/Sensing Thresholds**. After the leads have been implanted and before they are connected to the device, separately identify and document the baseline morphology for capture and sensing thresholds for each ventricular lead. Once baselines are established, determine if the ECG or IEGM recordings can help discriminate biventricular capture, and negative depolarizations for each lead. In a cardiac resynchronization therapy system, the ECG may display two distinct capture loss morphologies, because the left and right chambers often have different pacing thresholds. To ensure that the device is losing capture on both sides of the heart, allow the test to run until a marked change in morphology occurs, indicating capture loss on both sides.
- **Device Testing with PSA.** Before implantation of the device, the clinician may wish to test the device using a compatible PSA with calibrated sensitivity and output settings. When the probe is attached to the pulse generator's connector, the programmed parameters should be identical to the Shipped Settings listed on the package label and in Table 21 on page 71.

Implantation

- **Ventricular Leads with Polished Platinum Tip Electrodes.** Pairing a ventricular lead with a polished platinum tip electrode with a ventricular lead with a tip electrode of a different material may create a source impedance mismatch that could adversely affect sensing.
- **Case Markings.** Examine the markings on the device case and verify proper atrial, left and right ventricular connections.
- **Setscrew.** Exercise caution when turning the setscrew, which may be backed out of the connector if turned counter-clockwise for more than two rotations.
- **RV Lead.** An RV lead must be used with the Frontier™ II Cardiac Resynchronization Pacing System. Back-Up VVI pacing is delivered to the right ventricle only.

Programming

- **Programmer.** The Frontier™ II device can be interrogated and programmed with the Model 3510 programmer[2] with Model 3307 software version 4.8 or higher. For a list of programmable parameters and their programmable values, see Table 22 on page 75.
- **Setting Lead Type.** When the user interrogates the device for the first time, the programmer will prompt the user to set the Lead Type. Because some parameters are determined by the Lead Type (for example, Pulse Configuration), the user should set this parameter when the device is implanted. See Ventricular Lead Selection on page 60.
- **Lead Impedance Values.** Independent lead impedance values are displayed for the RV and LV leads.
- **Ventricular Pulse Amplitudes and Pulse Widths.** The right and left ventricular pulse amplitudes and pulse widths are independently programmable. The pulse amplitude and pulse width should be evaluated in each chamber accordingly. Typically, capture thresholds are higher in the left ventricle.
- **Follow-up Capture Threshold Measurements.** The RV and LV ventricular capture threshold measurements are evaluated independently. During an RV or LV ventricular capture test, the clinician may be able to determine when capture is occurring by noting changes in the ECG morphology. See the Bradycardia Devices Reference Manual for more information.
- **Emergency VVI.** When programming the device to Emergency VVI settings, press the programmer's Emergency VVI button only once. Settings for Emergency VVI can be found in the Bradycardia Devices Reference Manual or by selecting the HELP button on the Model 3510 Programmer.
- **AOO(R), VOO(R), and DOO(R) Modes** are primarily intended for temporary diagnostic use. Long-term use may result in competitive pacing, inducing potentially dangerous arrhythmias.

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[2] The Frontier II device can not be used with the Model 3500 programmer.

- **ODO, OVO, and OAO Modes** are not recommended for patients who would be adversely affected by even a short cessation of pacing.
- **Noninvasive EP Testing.** Atrial or ventricular tachycardia or fibrillation may occur during noninvasive EP testing. Therefore, (1) closely monitor the patient, and (2) have emergency equipment for cardioversion/defibrillation readily available while conducting EP testing.
- **Pulse Amplitude.** If the lead is implanted in the atrium, determine the capture threshold before programming the Pulse Amplitude. Program Pulse Amplitude to yield a suitable safety margin for reliable, long-term capture. Reassess capture thresholds periodically.
- **High-Output Settings.** Programming high-output settings with a high Base Rate may shorten the time to ERI.
- **Runaway Protection**. Hardware circuitry in the device prevents the device from pacing at rates higher than 190 ppm (± 10 ppm). When the device is pacing in a biventricular configuration, the device software provides the runaway protection.
- **Sensing Configuration**. Sensing tests should be performed whenever changes are made to the sensing configuration. For more information on performing sensing tests, see Sense Threshold Test on page 13-25.
- **Sensitivity Settings.** Careful consideration should be given to patient exposure to electromagnetic interference if programming sensitivity greater than 0.3 mV with a bipolar sense configuration setting and 2.0 mV with a unipolar sense configuration setting.

Environmental and Medical Therapy Hazards

St. Jude Medical® devices are equipped with special shielding and filters which significantly reduce the adverse effects of electromagnetic interference (EMI) on the operation of the device.

Patients should be directed to exercise reasonable caution in avoidance of strong electric or magnetic fields. If the device inhibits or reverts to asynchronous operation while in the presence of electromagnetic interference (EMI), the patient should move away from the EMI source or turn the source off.

Advise patients to seek medical guidance before entering environments which could adversely affect the operation of the device, including areas protected by a warning notice preventing entry by patients with pacemakers.

Medical Procedures and Environments

In general, patients with pacemakers should not be exposed to hospital equipment that produces high electromagnetic field strength signals, such as diathermy machines and electrosurgical units.

- **External Defibrillation.** The electronic circuitry in the device provides protection from defibrillation discharges. Nevertheless, do not place defibrillator paddles

directly over the device or pacing lead. Following defibrillation, ensure that the pacemaker is operating correctly.

- **Magnetic Resonance Imaging (MRI).** MRI for patients with implantable pulse generators has been contraindicated by MRI manufacturers. Clinicians should carefully weigh the decisions to use MRI with pacemaker patients. Additional safety concerns include:
    - Magnetic and RF fields produced by MRI may increase pacing rate, inhibit pacing, cause asynchronous pacing or result in pacing at random rates
    - MRI may result in changes in capture thresholds due to heating of pacing leads in any patient
    - MRI may irreversibly damage the pulse generator
    - Patients should be closely monitored during the MRI
    - Assess the pulse generator function before and after exposure to MRI.
- **Ionizing Radiation.** Therapeutic ionizing radiation (for example, used in linear accelerators and cobalt machines) can permanently damage the device's circuitry. The effect of ionizing radiation is cumulative; the potential for damage to the device is proportional to the patient's total radiation dosage. If the patient must be exposed to ionizing radiation, protect the device during the procedure with local radiation shielding. If tissue near the implant site must be irradiated, it may be necessary to move the device to another area. Before and after exposure to radiation, evaluate the device operation to identify any adverse consequences.
- **Transcutaneous Electrical Nerve Stimulation (TENS).** To reduce the possibility of interference with pacemaker function, place the TENS electrodes close to one another and as far from the device as possible. Before allowing unrestricted use of TENS in a home or other setting, screen the patient in a monitored environment for possible interaction.
- **Therapeutic Diathermy.** Avoid diathermy, even if the device is programmed off, as it may damage tissue around the implanted electrodes or may permanently damage the device.
- **Electrosurgical Cautery** can induce ventricular arrhythmias and/or fibrillation or may cause asynchronous or inhibited device operation. If use of electrocautery is necessary, the current path and ground plate should be kept as far away from the device and leads as possible. A bipolar cauterizer may minimize these effects. Following electrocautery, conduct a thorough assessment of the device.
- **RF Ablation.** Radiofrequency (RF) ablation in patients with a device may cause any of the following: asychronous pacing above or below the programmed rate; reversion to an asynchronous operation; device electrical reset; or premature triggering of the elective replacement indicator.

  RF ablation risks may be minimized by: programming a non-rate responsive, asynchronous pacing mode prior to the RF ablation procedure; avoid direct contact between the ablation cather and the implanted lead or device; positioning the ground plate so that the current pathway does not pass through or near the device system, i.e., place the ground plate under the patient's buttocks or legs;

having a programmer available for temporary pacing; or having external defibrillation equipment available.

Patient Environment

- **High-Voltage** transmission lines and equipment, arc or resistance welders, induction furnaces, and similar equipment may generate substantial EMI fields that may interfere with device operation.
- **Communication Equipment**, such as microwave transmitters,[3] linear power amplifiers, or high-power amateur transmitters may generate sufficient EMI to interfere with the operation of the device. Advise patients to move away from this equipment to resume normal pacemaker operation.
- **Home Appliances** that are in good working order and properly grounded do not usually produce enough EMI to interfere with device operation. Electric vibrators, razors, and handtools held directly over the device may disturb its operation.
- **Twiddler's Syndrome.** Caution patients against manipulating the implanted device since it may result in lead damage or lead displacement.
- **Patient Activities.** Any activities that involve repetitive impacts or jarring (such as horseback riding, jackhammer use, etc.) may increase the pacing rate when the device's Sensor is programmed On. Caution patients against such activity and program Sensor parameters with these activities in mind.
- **Theft Detection Systems.** Theft detection systems, such as those often located at the entrances and exits of stores and public libraries, may disturb pacemaker function only if the patient pauses in the field path.
- **No Pacer Symbol.** Caution patients implanted with this device to avoid areas marked with the NO PACER symbol.

Figure 3. No Pacer Symbol

- **Cellular Phones.** A St. Jude Medical-designed protective filter in the device prevents cellular phone-generated electromagnetic signals from interfering with the operation of the device.[4]

  Clinical tests performed by St. Jude Medical and five independent organizations[5] have documented that devices incorporating this protective filter are not affected

[3] Home appliance microwave ovens do not interfere with device operation.

[4] Carrillo R, Williams DB, Traad EA, Schor JS. Electromagnetic filters impeded adverse interference of pacemakers by digital cellular telephones. *JACC* 1996; 27(2A):15A Abstract 901-22.

by any known analog cellular phone systems or any of the digital cellular phone technologies listed in Table 2.

Type	Description
NADC (TDMA 50)	North American Digital Communications (Time Division Multiple Access 50 Hz)
US (TDMA 11)	Time Division Multiple Access 11 Hz
CDMA	Code Division Multiplex Access
PCS (GSM 1.9 GHz)	Personal Communication Systems (GSM 1.9 GHz)

Table 2. Digital Phones Standards Tested

No special precautions are required for patients using the cellular phones listed above. Phone systems not listed in Table 2 have not been tested, and their interaction with the device cannot be guaranteed.[5]

The device has also been tested for compatibility with handheld transmitters in accordance with the requirements of AAMI PC69. This testing covered the operating frequencies (450 MHz - 3 GHz) and pulsed modulation techniques of all of the digital cellular phone technologies in worldwide use today. For more information, you or your patient may wish to contact Technical Support (page 85) to obtain more information on the interaction of certain cellular phones and this device.

Explantation

- Do not reuse explanted devices and leads.
- Clean explanted equipment with +1% sodium hypochlorite, rinse with water, dry.
- Return the explanted device to the manufacturer.
- Explant the device before cremation of a deceased patient.
- Hex wrenches are available for disconnecting a previously implanted device from the indwelling leads. To obtain the wrenches, contact your local St. Jude Medical representative.

Adverse Events

The safety data presented in this section includes data from the Post AV Node Ablation Evaluation (PAVE) study which received approval under PMA P030035. Based on the results of the PAVE study, the biventricular pacing system is being legally marketed for "maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic atrial fibrillation and have NYHA Class II or III heart

[5] Center for Devices and Radiological Health, FDA, Rockville MD; Medical Devices Bureau of Health, Ottawa, Ontario, Canada; Mount Sinai Medical Center of Greater Miami, Miami Beach FL; Center for Study of Wireless Electromagnetic Compatibility, University of Oklahoma, Norman OK; Qualcomm, Inc., San Diego, CA.

failure". The identical CRT-P system as was approved in PAVE was under study with the Ventricular Resynchronization Therapy Randomized Trial (VecToR) (IDE G000229) with the goal to obtain additional labeling for heart failure. The PAVE safety data is therefore presented with the VecToR safety data for completeness.

The PAVE clinical study began on August 16, 2000. As of August 5, 2003, (PMA clinical report date) there were 361 attempted implants in the PAVE (Post-AV Node Ablation Evaluation) study from centers in the United States and Canada with average implant duration of 13.0 months (range: 0.1 - 35.7 months).

Although the VecToR (Ventricular Resynchronization Therapy Randomized Trial) clinical study was conducted using the identical Frontier™ system as in the PAVE study, all Frontier devices including the Frontier II device have equivalent CRT functionality. The VecToR study began on October 11, 2000. As of September 7, 2004, there were 144 attempted implants, of which 120 were successful, from centers in the United States and Canada with average implant duration of 22.7 months (range: 0.1 - 45.3 months).

Death information was gathered and classified by an independent mortality committee of three practicing physicians according to a published classification scheme. A summary of the death classification from the PAVE and the VecToR studies are shown on pages 3 and 5.

Observed Adverse Events

The PAVE and VecToR studies' cumulative implant duration for all enrolled patients was 7,948 months with a mean of 15.7 ± 12.2 months (range of 0.1 to 45.3 months). The cumulative duration for patients in the investigational group (all patients from PAVE and VecToR except the RV group in the PAVE study) was 6,393 months (532.8 years).

During the entire study period for both studies, 230 adverse events were reported for the investigational group including 80 complications and 150 observations. Tables 6 and 7 summarize the complications and Table 8 summarizes the observations that occurred during the studies. System-related complications and observations are based on patients with the investigational system only (PAVE, N = 254; VecToR, N = 144; Total, N = 398). Procedure-related complications are based on total number of attempted implants (PAVE, N = 255; VecToR, N = 144; Total, N = 399).

An Adverse Event is defined as an unfavorable clinical event, which impacts, or has the potential to impact, the health or safety of a clinical study participant caused by, or associated with, a study device or intervention. An adverse event is classified as a Complication when it results in an injury or an invasive intervention (for example, lead repositioning after lead dislodgement) that would not have occurred in the absence of the implanted device and/or system components. An Observation is defined as an adverse event that is not associated with injury to the patient or an invasive intervention, but which is associated with the system under investigation, or the programming thereof.

PAVE Study

Primary Cause	RV (N=106)	BV (N=146)	LV (N=53)	Roll-in (N=56)	Total (N=361)
Cardiac: Arrhythmic	1	1	1	0	3
Cardiac: Other	7	3	3	2	15
Cardiac: Unknown	0	1	0	0	1
Non-Cardiac	4	2	5	4	15
Unknown	6	5	3	2	16
Total	**18**	**12**	**12**	**8**	**50**[6]
% Death	**17.0**	**8.2**	**22.6**	**14.3**	**13.8**

Table 3. All Deaths Reported in the PAVE Study

VecToR Study

A summary of the death classification through the first 6-months post-implant is shown in Table 4 below.

Primary Cause	ON (N=59)	OFF (N=47)	Roll-in (N=38)	Total (N=144)
Non Sudden Cardiac	1	0	2	3
Sudden Cardiac	0	1	0	1
Non Cardiac	0	0	1	1
Total	**1**	**1**	**3**	**5**
% Death	**1.7**	**2.1**	**7.9**	**3.5**

Table 4. Deaths as Randomized Through Six Months

Table 5 lists the additional 20 total deaths reported that occurred after 6 months post-implant. Since all patients received the identical system and cross-over was allowed after 6 months, data was not stratified by treatment assignment.

Primary Cause	Total (N=144)
Non Sudden Cardiac	8[7]
Sudden Cardiac	3
Non Cardiac	4
Unknown	2

[6] One additional patient was consented, but died prior to any study related procedure.

[7] One death was felt to be related to the procedure by the independent external mortality committee, but not attributed to any components of the investigational system.

Unknown Presumed Sudden	2
Unknown-Sudden	1
Total	**20**
% of Patients	**13.8%**

Table 5. All Deaths Reported for Vector Study Beyond Six Months Post-Implant

An Adverse Event is defined as an unfavorable clinical event, which impacts, or has the potential to impact, the health or safety of a clinical study participant caused by, or associated with, a study device or intervention. An adverse event is classified as a Complication when it results in an injury or an invasive intervention (for example, lead repositioning after lead dislodgement) that would not have occurred in the absence of the implanted device and/or system components. An Observation is defined as an adverse event that is not associated with injury to the patient or an invasive intervention, but which is associated with the system under investigation, or the programming thereof.

During the entire study period for both studies, 230 adverse events were reported for the investigational group including 80 complications and 150 observations. Tables 6 and 7 summarize the complications and Table 8 summarizes the observations that occurred during the studies. System-related complications and observations are based on patients with the investigational system only (PAVE, N = 254; VecToR, N = 144; Total, N = 398). Procedure-related complications are based on total number of attempted implants (PAVE, N = 255; VecToR, N = 144; Total, N = 399).

Events	No. of Events	No. of Patients	% of Patients	Events/Device Months[8]
LV Lead Related:	**36**	**34**	**8.5**	**0.0056**
Acute LV Lead Dislodgement	11	11	2.8	0.0017
High Implant Thresholds (LV Lead)	8	8	2	0.0013
Diaphragmatic Stimulation	7	7	1.8	0.0011
LV Lead Loss of Capture	5	5	1.3	0.0008
High Pacing Thresholds (LV Lead)	2	2	0.5	0.0003
Chronic LV	1	1	0.3	0.0002

[8] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups for PAVE and the ON, OFF and Roll-in groups for VecToR. The cumulative duration in months in these groups was 6,393 months.

Lead Dislodgement				
LV Lead Fracture	1	1	0.3	0.0002
Pectoral Stimulation	1	1	0.3	0.0002
RA/RV Lead Related:	**8**	**7**	**1.8**	**0.0013**
Acute RA/RV Lead Dislodgement	4	3	0.8	0.0006
Chronic RA Lead Dislodgement	1	1	0.3	0.0002
RV Perforation	1	1	0.3	0.0002
RV Insulation Failure	1	1	0.3	0.0002
Lead Fracture (RA Lead)	1	1	0.3	0.0002
System - Other:	**4**	**4**	**1**	**0.0006**
Inadequate Lead Connection	2	2	0.5	0.0003
Ventricular Tachycardia	1	1	0.3	0.0002
Erosion (Pocket Erosion)	1	1	0.3	0.0002
Total System-Related	**48**	**41**	**10.3**	**0.0075**

Table 6. System-Related Complications for Investigational Group[9, 10, 11]

Events	No. of Events	No. of Patients	% of Patients	Events/Device

[9]Each patient may have more than one complication in more than one category.

[10]System-related complications based on total number of attempted implants (N = 398).

[11]The Investigational Group consists of all patients from the PAVE and VecToR studies except the RV group from the PAVE study.

[12] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups for PAVE and the ON,

				Months[12]
Procedure Related:	**32**	**30**	**7.5**	**0.005**
Coronary Sinus Dissection During Implant	13	13	3.3	0.002
Pneumothorax	4	4	1	0.0006
CS Perforation at Implant	3	3	0.8	0.0005
Pericardial Effusion	2	2	0.5	0.0003
Ventricular Tachycardia at Implant	2	2	0.5	0.0003
Tamponade	2	2	0.5	0.0003
Complete Heart Block at Implant	1	1	0.3	0.0002
Cardiopulmonary Arrest at Implant	1	1	0.3	0.0002
Non-Sudden Cardiac Death	1	1	0.3	0.0002
Pulmonary Edema Post Ablation	1	1	0.3	0.0002
LV Lead Dislodgment During Ablation	1	1	0.3	0.0002
Hemothorax	1	1	0.3	0.0002
Total System-Related and Procedure-Related Complications	**80**	**70**	**17.5**	**0.0125**

Table 7. Procedure-Related Complications for Investigational Group[13, 14, 15]

OFF and Roll-in groups fro VecToR. The cumulative duration in months in these groups was 6,393 months.

[13]Each patient may have more than one complication in more than one category.

[14]Procedure-related complications based on total number of attempted implants (N = 399).

Events	No. of Events	No. of Patients	% of Patients	Events/Device Months[16]
Diaphragmatic Stimulation	35	29	7.3	0.0055
Pectoral Stimulation	19	17	4.3	0.003
High Pacing Threshold (LV Lead)	18	18	4.5	0.0028
High Implant Thresholds (LV Lead)	10	10	2.5	0.0016
Loss of Capture (LV Lead)	9	9	2.3	0.0014
Hematoma at Implant	8	8	2	0.0013
CS Dissection	6	6	1.5	0.0009
Fatigue	6	6	1.5	0.0009
Infection	6	6	1.5	0.0009
Heart Failure - Worsening	3	3	0.8	0.0005
Telemetry Error	3	2	0.5	0.0005
Oversensing	3	3	0.8	0.0005
Discomfort - Device Site	2	2	0.5	0.0003
Thrombosis	2	2	0.5	0.0003
VVI Back-Up	2	2	0.5	0.0003
Stuck Stylet	2	2	0.5	0.0003
Undersensing (RA Lead)	1	1	0.3	0.0002
Loss of Capture-Intermittent (LV Lead)	1	1	0.3	0.0002
Hypotension	1	1	0.3	0.0002
Palpitation	1	1	0.3	0.0002

[15]The Investigational Group consists of all patients from the PAVE and VecToR studies except the RV group from the PAVE study.

[16] Events per Device-Month calculated as number of events divided by the total device cumulative duration in months in BV, LV and Roll-in groups for PAVE and the ON, OFF and Roll-in groups fro VecToR. The cumulative duration in months in these groups was 6,393 months.

Arrhythmia - Torsades	1	1	0.3	0.0002
Noise on IEGM	1	1	0.3	0.0002
Dyspnea on Exertion	1	1	0.3	0.0002
RV Back-up Pacing Due to PVCs	1	1	0.3	0.0002
Acute LV Lead Dislodgment (minor)	1	1	0.3	0.0002
RV Loss of Capture	1	1	0.3	0.0002
LV Lead Undersensing	1	1	0.3	0.0002
Medication Reaction	1	1	0.3	0.0002
Pneumothorax	1	1	0.3	0.0002
CS Perforation	1	1	0.3	0.0002
Pre-Syncope	1	1	0.3	0.0002
Syncope	1	1	0.3	0.0002
Total Events	**150**	**112**	**28.1**	**0.0235**

Table 8. Observations for Investigational Group[17, 18, 19]

Potential Adverse Events

Potential adverse events associated with the use of the transvenous leads and pacing systems include:

- Body rejection phenomena
- Cardiac/coronary sinus dissection
- Cardiac/coronary sinus perforation
- Cardiac tamponade
- Coronary sinus or cardiac vein thrombosis
- Death
- Device migration and pocket erosion

[17]Each patient may have more than one observation in more than one category.

[18]Observations based on total number of attempted implants (N = 398).

[19]The Investigational Group consists of all patients from the PAVE and VecToR studies except the RV group from the PAVE study.

- Endocarditis
- Excessive bleeding
- Hematoma/seroma
- Induced atrial or ventricular arrhythmias
- Infection
- Local tissue reaction; formation of fibrotic tissue
- Loss of pacing and/or sensing due to dislodgment or mechanical malfunction of the pacing lead
- Myocardial irritability
- Myopotential sensing
- Pectoral/diaphragmatic/phrenic nerve stimulation
- Pericardial effusion
- Pericardial rub
- Pneumothorax/hemothorax
- Pulmonary edema
- Rise in threshold and exit block
- Thrombolytic or air embolism
- Valve damage

The following in addition to the above, are potential complications associated with the use of rate modulated pacing systems.

- Inappropriate, rapid pacing rates due to sensor failure or to the detection of signals other than patient activity.
- Loss of activity-response due to sensor failure.

A coronary sinus venogram is unique to lead placement in the cardiac venous system, and carries risks, such as renal failure, cardiac or coronary sinus dissection, and cardiac or coronary sinus perforation.

Potential complications reported with direct subclavian venipuncture include hemothorax, laceration of the subclavian artery, arteriovenous fistula, neural damage, thoracic duct injury, cannulation of other vessels, massive hemorrhage, and rarely death.

Summary of Clinical Investigations

PAVE Study

A prospective, randomized, controlled, multi-center clinical trial conducted at 49 participating sites (44 in the US, 5 in Canada) compared the safety and effectiveness results for patients receiving the Frontier™ Model 5508 pulse generator and the Aescula™ 1055K Left Heart Lead to those receiving legally marketed right ventricular pulse generators and standard leads following an AV nodal ablation for chronic atrial fibrillation. Chronic AF is defined as persisting without interruption for at least one month.

The study's cumulative implant duration for all enrolled patients was 4,684 months with a mean of 13.0 ± 9.6 months (range of 0.1 to 35.7 months). Two hundred and six patients underwent successful LV lead placement. The cumulative duration for all investigational patients (BV, LV and Roll-in groups only) was 3,129 months.

For this randomized study, the key inclusion criteria were:

- Patients who will undergo complete AV nodal ablation for chronic atrial fibrillation (defined as persisting without interruption for at least one month) resulting in complete AV block
- Patients who are on a stable medical therapy regimen, and
- Patients who are able to complete the six-minute walk with the only limiting factor(s) being fatigue and/or shortness of breath.

Key study exclusion criteria were:

- Patients who are classified as NYHA Class IV
- Patients who can walk > 450 meters in six-minute walk test
- Patients who have an implanted ICD or being considered for implant of an ICD
- Patients with prosthetic valve replacements
- Patients with severe musculoskeletal disorder(s). and
- Patients who cannot independently comprehend and complete the quality of life questionnaire.

The overall study population included 361 patients. One hundred and forty-six were randomized to BV, and 106 were randomized to RV. In addition, 53 were randomized to LV pacing under a previous revision of the investigational plan. Fifty-six were "Roll-in" patients (nonrandomized) and received the biventricular pacing system (Frontier pulse generator and Aescula lead system). All patients had permanent pacemaker implant indication following an elective AV nodal ablation for chronic atrial fibrillation. The mean age was 69.2 ± 10.0 years; 34.3% were female and 65.7% were male. Fifteen percent of the patients had no diagnosis of heart failure or were NYHA Class I, 48% were NYHA Class II, and 37% were NYHA Class III prior to implant. Safety data from all patients were reported.

Primary Objectives and Results

1. Freedom from system-related complications through six months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from system-related complications for the BV group will not be less than 70%. A system-related complication was defined as a complication that is caused by a failed pacing system. A pacing system refers to all implanted components, including the pulse generator, leads, and the interaction of these components.

Results: There were 29 system-related complications in 26 patients within six months follow-up. The freedom from system-related complications is 87.8% with a lower bound of 84.0%. Objective met.

2. Freedom from pulse generator-related complications through six months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from pulse generator-related complications for the BV group through six months will not be less than 90%.

Results: There were no pulse generator-related complications through six months. The survival rate is 100% with a lower bound of 98.6%. Objective met.

3. Freedom from Aescula™ lead-related complications through six months

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula™ lead-related complication for the BV group through six months will not be less than 75%.

Results: There were 25 Aescula lead-related complications in 24 patients through six months follow-up. The freedom from Aescula lead-related complications is 88.2% with a lower bound of 84.4%. Objective met.

4. Rate of successful implantation of the Aescula™ lead

Objective: The lower bound of the one-sided 95% confidence interval of the successful implantation rate of the Aescula lead for the BV group will not be less than 80%. The success rate was defined as the proportion of patients who received the complete pacing system.

Results: One hundred and forty-six patients randomized to BV underwent attempted implants. One hundred and twenty-five were successfully implanted. The rate of successful implant of the Aescula lead for BV group is 86% with a lower bound of 81%. Objective met.

5. Aescula™ lead pacing threshold at six months

Objective: The upper bound of the one-sided 95% confidence interval of mean capture threshold will not be greater than 3.0 V for the BV group at six months.

Results: The pacing threshold at six months for the BV group is 2.27 V ± 1.66 V with an upper bound of 2.53 V. Objective met.

6. Exercise capacity as measured by distanced walked in six-minute walk test

Objective: To determine if the treatment group (BV) shows a statistically significant improvement over the control group (RV) at the six months follow-up time.

Results: The treatment group (BV) showed statistically significant improvement over the control group (RV) in distance walked from pre-implant to six months (p = 0.03). The BV group also had a greater percentage of patients showing improvements than the RV group (p = 0.035). Figure 4 illustrates the improvement in the six-minute walk between BV and RV groups. Table 9 outlines the improvement distribution in the six-minute walk between BV and RV groups.

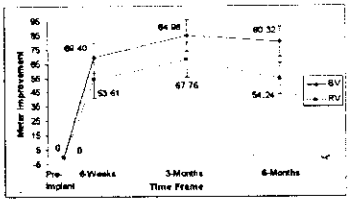


Figure 4. Improvements in Six-Minute Walk Distance in BV and RV Groups (p = 0.03)

	RV (N = 66)	BV (N = 84)
Improved (> 5 m)	46 (69.70%)	69 (82.14%)
No Change (–5 to 5 m)	4 (6.06%)	4 (4.76%)
Worsened (< –5 m)	16 (24.24%)	11 (13.10%)

Table 9. Distribution of Improvement in BV and RV Group in Six- Minute Walk (p = 0.035)

Secondary Objectives and Results

1. Quality of life as measured by SF-36 score

Objective: To determine if the BV group shows improvement over the RV group at the six-month follow-up in the health-related quality of life as measured by the SF-36 score.

Results: Using the SF-36 Quality-of-Life questionnaire, a standardized measurement of quality of life, the study found that for the six-week to six-month visit time period, the improvement in SF-36 scales was not different between groups.

2. Functional capacity as measured by peak VO_2

Objective: To determine if the BV group shows improvement in functional capacity, as measured by peak VO_2, from the six-week follow-up to the six-month follow-up.

Results: The BV group showed an improvement of 0.86 ml/kg/min in peak VO_2 from six weeks to six months measured during CPX testing (p = 0.03). The BV group also had a greater percentage of patients showing improvement in peak VO_2 (p = 0.02). Figure 5

illustrates the improvement in peak VO_2 in BV and RV groups. Table 10 outlines the distribution of improvement in peak VO_2 between BV and RV groups.

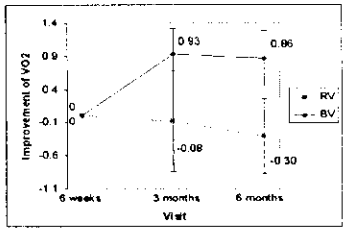


Figure 5. Improvements in Peak VO_2 in BV and RV Groups ($p = 0.03$ Within BV Group)

Change in Peak VO_2 (ml/kg/min)	RV (N = 10)	BV (N = 35)
Improved (> 0.5)	4 (40%)	21 (60.0%)
No Change (–0.5 to 0.5)	0 (0%)	4 (11.4%)
Worsened (< –0.5)	6 (60%)	10 (28.6%)
p-Value Within Group	0.38	0.02

Table 10. Distribution of Improvements in VO_2 in BV and RV groups

VecToR Study

The VecToR CRT-P study was designed to pursue approval for cardiac resynchronization therapy for a Heart Failure (HF) patient population, which, in the investigators' opinion, does not need the additional benefit of back up defibrillation. An identical system (i.e., Frontier biventricular pacing system) as used in the PAVE population was used in the VecToR CRT-P population. The safety data presented shows that the system is safe for its intended use and demonstrates the safety of the Frontier CRT-P system.

The VecToR (CRT-P) study did not enroll sufficient numbers of randomized patients to meet its effectiveness objectives. Although the VecToR (CRT-P) study and the RHYTHM (CRT-D) study used different pulse generators (Frontier and Epic HF, respectively), both used the same biventricular pacing function which is delivered through the legally marketed SJM Aescula lead to provide cardiac resynchronization therapy. Data from the RHYTHM Study is used to demonstrate CRT effectiveness, as the patient populations in RHYTHM and VecToR are comparable.

The VecToR study was a prospective, double-blind, randomized, controlled, multi-center clinical trial of patients with New York Heart Association Class III/IV congestive heart failure, and was conducted at 41 participating sites (39 in the US, 2 in Canada). The study compared the safety and effectiveness of cardiac resynchronization pacing therapy (CRT-P), using the Frontier Model 5508 pulse generator and the Aescula 1055K Left Heart Lead to no CRT-P therapy.

Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

1. Symptomatic ischemic or nonischemic dilated cardiomyopathy, which is not due to reversible causes.
2. Left ventricular end-diastolic diameter >54mm as measured by echocardiography.
3. Left ventricular ejection fraction ≤ 35% as measured by echocardiography.
4. QRS duration of ≥140 ms.
5. Stable but advanced heart failure due to left ventricular dysfunction (diagnosed for at least 6 months) despite stable conventional medical therapy.
6. Completed the 6-minute walk test as outlined in the protocol with the only limiting factor(s) being fatigue and/or shortness of breath.
7. Adequate cardiographic acoustic windows.
8. Provided informed consent for study participation and, are willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Exclusion Criteria

1. Can walk >450 meters during the 6-minute walk test.
2. Have standard bradycardia indications or likely to need pacing within the next 6-months.
3. Are classified as NYHA Class I or II.
4. Have a history of persistent or chronic atrial fibrillation or a history of atrial fibrillation which required intervention to revert to normal sinus rhythm.
5. Have an implanted cardioverter defibrillator (ICD) or, are being considered for implantation of an ICD.
6. Are contraindicated for an emergency thoracotomy.
7. Are considered status 1 for cardiac transplantation and are likely to receive transplantation within 1 year
8. Are being treated with parenteral inotropic agents (e.g., dobutamine) or have been treated with such agents within the past 30 days.
9. Have prosthetic valve replacement(s).
10. Have severe musculoskeletal disorder(s).
11. Are under the age of 18 years.
12. Are pregnant or plan a pregnancy in the next 6 months.
13. Are currently participating or participated within the past 30 days in any clinical investigation.
14. Have a life expectancy of less than 6 months.
15. Cannot independently comprehend and complete the Minnesota Living With Heart Failure questionnaire.
16. Are allergic to dexamethasone sodium phosphate (DSP).

To gain initial experience, investigators were given the option of prospectively determining that the first two patients implanted would not be randomized and would not

count toward the implant success rate. However, these "Roll-In" patients met all inclusion criteria, were blinded to their treatment arm, and were followed per protocol. As such and as defined in the protocol, this "Roll-In" group is included in the safety analysis. All patients received the pacing system comprised of the investigational Frontier pulse generator and Aescula left heart lead, and a legally marketed right atrial and right ventricular lead. Patients were followed every 3 months for the first twelve months, and every six months thereafter. Patients in the CRT OFF group were allowed to cross over after completing the requirements of the 6-month visit.

As of September 7, 2004, the total time of follow-up from the time of successful implant in 120 patients was 2383 patient months. The average time of follow-up was 19.9 ± 8.9 (range 0.8 to 35.4) patient months.

Patient Population

The overall VecToR study population included 144 patients. Fifty-nine (59) patients were randomized to ON, and 47 patients were randomized to OFF. Revision C of the VecToR protocol excluded NYHA Class II patients. Thirty-eight (38) were "roll-in" patients (non-randomized) and received the cardiac resynchronization pacing therapy system (Frontier pulse generator and Aescula lead system). Safety analyses include all patients with the Frontier pulse generator and the Aescula left heart lead, including ON, OFF, and roll-in. The mean age was 67.1 ± 9.7 years and there were 62.5% male and 37.5% female. Twenty-nine percent (29%) of the patients were NYHA Class II, 65% were NYHA Class III, and 6% were NYHA Class IV prior to implant.

Primary Safety Objectives and Results

The primary safety objectives for the VecToR study are presented below.

1. FREEDOM FROM SYSTEM-RELATED COMPLICATIONS THROUGH SIX MONTHS

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from system-related complications will not be less than 70%. A system-related complication was defined as a complication that is caused by a failed pacing system. A pacing system refers to all implanted components, including the pulse generator, leads, and the interaction of these components.

Results: There were 12 system-related complications in 11 patients within six-months follow-up. The freedom from system-related complications is 90.7% with a lower bound of 86.4%. Objective met.

2. FREEDOM FROM PULSE GENERATOR-RELATED COMPLICATIONS THROUGH SIX MONTHS

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from pulse generator-related complications for the combined group through six months will not be less than 90%.

Results: There were no pulse generator-related complications through six months. The survival rate is 100% with a lower bound of 97.1%. Objective met.

3. FREEDOM FROM AESCULA™ LEAD-RELATED COMPLICATIONS THROUGH SIX MONTHS

Objective: The lower bound of the one-sided 95% confidence interval of the freedom from Aescula™ lead-related complication through six months will not be less than 75%.

Results: There were 8 Aescula lead-related complications in 8 patients through six-months follow-up. All patients from the VecToR study who were successfully implanted are included in this analysis. The freedom from Aescula lead-related complications is 93.3% with a lower bound of 89.5%. Objective met.

4. RATE OF SUCCESSFUL IMPLANTATION OF THE AESCULA™ LEAD

Objective: The lower bound of the one-sided 95% confidence interval of the successful implantation rate of the Aescula lead will not be less than 80%. The success rate was defined as the proportion of patients who received the complete pacing system.

Results: A total of 144 patients who were randomized to CRT ON or OFF in the VecToR study and underwent attempted BV implants. One hundred and twenty (120) were successfully implanted. The rate of successful implant of the Aescula lead is 84% with a lower bound of 78% which does not meet the protocol defined objective for this endpoint (lower 95% confidence bound of 80%).

5. AESCULA™ LEAD PACING THRESHOLD AT SIX MONTHS

Objective: The upper bound of the one-sided 95% confidence interval of mean capture threshold will not be greater than 3.0 V for the combined group at six months.

Results: The electrical performance data of the LV lead were available on a total of 110 patients at six months. The pacing threshold at six months for the LV lead is 2.10 V with an upper bound 95% confidence interval of 2.34 V. Objective met.

RHYTHM Study

The RHYTHM ICD Study demonstrated that the SJM CRT-D system (Epic HF and Aescula lead) was safe and effective in NYHA Class III and IV heart failure patients with prolonged QRS duration and served as the basis for the recent PMA approved (PMA # P030054). The RHYTHM ICD study enrolled patients who also had a current ICD indication, which at the time the study was initiated included patients who were indicated

for an ICD solely for primary prevention or prophylaxis (i.e., the patients were at risk of ventricular tachyarrhythmias and sudden death due to other clinical characteristics, but had not experienced a spontaneous or induced tachycardia).

The RHYTHM ICD study was a prospective, multicenter, randomized, double-blind, controlled clinical investigation designed to assess the safety and effectiveness of the Epic HF ICD system in patients who were indicated for implantable cardioverter defibrillation therapy with New York Heart Association Classification of III or IV and a prolonged QRS duration. The objective of this clinical study was to verify the safety and effectiveness of the Epic HF ICD (Model V-338) system in an ICD indicated patient population with advanced heart failure (NYHA Classification III or IV) and prolonged QRS duration.

Study Inclusion and Exclusion criteria are listed below:

Inclusion Criteria

1. Approved indication for implantation of an ICD for treatment of a life-threatening ventricular tachyarrhythmia(s).
2. Symptomatic, advanced heart failure (ischemic or non-ischemic) not due to reversible causes, diagnosed for at least 6-months.
3. New York Heart Association (NYHA) Classification of III or IV, despite receiving a minimum of 90 days of appropriate pharmacological therapy.
4. Receive optimal pharmacological therapy for CHF (including angiotensin converting enzyme inhibitor and beta blocker, as tolerated) which has been stable during the 30 days prior to enrollment.
5. Left ventricular ejection fraction (LVEF) $\leq 35\%$.
6. Ventricular conduction delay manifested as a QRS duration ≥ 150 msec.
7. Ability to complete cardiopulmonary exercise stress testing and 6-Minute hall walk test, with the only limiting factor(s) being fatigue and/or shortness of breath.
8. Ability to independently comprehend and complete a quality of life questionnaire (Minnesota Living with Heart Failure).
9. Ability to provide informed consent for study participation and be willing and able to comply with the prescribed follow-up tests and schedule of evaluations.

Exclusion Criteria

1. Standard bradycardic indication for pacing.
2. History of chronic atrial fibrillation (continuous AF lasting > 1 Month) within 1 year prior to enrollment or have undergone cardioversion for AF in the past month.
3. Ability to walk > 450 meters during the 6-Minute walk test.
4. NYHA Classification of I or II.
5. Contraindication for an emergency thoracotomy.
6. Classification of Status 1 for cardiac transplantation or consideration for transplantation over the next 6-months.

7. Recent myocardial infarction, unstable angina or cardiac revascularization (PTCA or CABG) within 1 month of enrollment.
8. Recent CVA or TIA - within 3 months of enrollment.
9. Severe musculoskeletal disorder(s).
10. Pregnant or a planning for pregnancy in next 6-months.
11. Currently participating in, or has participated in any clinical investigation within the last 30 days. (the only exception being that of a registry trial)
12. Life expectancy of less than 6-months.
13. Less than 18 years of age.

All patients who met enrollment criteria underwent implantation of the Epic HF ICD system and a St. Jude Medical left ventricular pacing lead. ICD therapy was activated at the time of implant for all patients. Patients underwent Baseline evaluation between two weeks and 30 days following successful device implantation. Baseline was considered time zero for the purposes of evaluation of resynchronization study endpoints.

Patients were randomized following completion of Baseline testing and were assigned to either the treatment group (CRT ON) or the control group (CRT OFF) at a 2:1 ration. Patients who underwent unsuccessful implantation of the Epic HF ICD system were followed for a period of 30 days prior to withdrawal from the study. All patients who were successfully implanted were followed at 1, 3, 6 and every 3 months thereafter until the study was completed. Cross-over from the control group was allowed after completing the 6-month visit.

As of March 17, 2004, the total time of follow-up from the time of successful implant was 2205 patient months. The average time of follow-up was 12.1 ± 3.4 (range 0.3 to 20.3) patient months.

Patient Population

Of the 205 patients enrolled in the RHYTHM ICD study, one hundred and eighty-three (183) lead implant attempts were successful (180 successful on the first attempt and 3 successful on the second attempt). One additional patient had a successful left ventricular lead implant, but had high defibrillation thresholds. This patient was withdrawn from the study and received a heart transplant, leaving a total of 182 successful system implants.

Patients who were successfully implanted with the Epic HF ICD system had a Baseline visit approximately two weeks after implant, during which the following tests/assessments were performed: Electrical measurements on RA, RV and LV leads, cardiopulmonary exercise (CPET) test, echocardiogram, NYHA class assessment, 6 minute walk test, and Minnesota Living with Heart Failure questionnaire. Of the 182 patients with successful implants, two patients expired and one patient withdrew from the study before the Baseline visit and therefore, 179 patients had a Baseline visit. One additional patient who had a Baseline follow-up visit refused randomization and all the Baseline evaluations except device interrogation and electrical measurements, but

remained in the study. Therefore, a total of 178 patients completed the requirements of the Baseline visit.

Primary Effectiveness Objective and Results

CARDIAC RESYNCHRONIZATION THERAPY EFFECTIVENESS (PEAK VO_2)

Objective: To determine if the treatment group (CRT ON) shows a statistically significant improvement over the control group (CRT OFF) at six months.

Results: In the intention-to-treat analysis, patients who crossed over from the CRT OFF group to the CRT ON group during the study were analyzed according to the original treatment group they belonged to. Table 11 contains a summary of the improvement in peak VO_2 values in the two treatment groups for this analysis. The average improvement in the CRT ON group over the CRT OFF group was approximately 1.9 ml/kg/min. The p-value was 0.001. Objective met.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	12.8 ± 3.7	11.2 ± 3.0
6-months	11.4 ± 5.6	11.7 ± 3.2
Change	-1.41 ± 4.6	0.52 ± 2.5
Overall improvement in CRT ON vs. CRT OFF = 1.9 ml/Kg/min		

Table 11. Improvement in Peak VO_2 Values (ml/kg/min) Intention-to-Treat Analysis (N=126)

Secondary Objective and Results

1. IMPROVEMENT IN NYHA CLASS AT 6-MONTHS OVER BASELINE

Objective: To determine if the treatment group (CRT ON) shows an improvement over the control group (CRT OFF) at six months.

Results: Table 12 shows the average change in NYHA Class from Baseline to 6-months for each group. Objective met.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	2.86 ± 0.52	3.01 ± 0.33
6-months	2.58 ± 0.73	2.53 ± 0.69
Change	-0.28 ± 0.63	-0.48 ± 0.65

Table 12. Baseline and Six Month NYHA Class (N=126)

2. IMPROVEMENT IN QUALITY OF LIFE AT 6-MONTHS OVER BASELINE

Objective: To determine if the treatment group (CRT ON) shows an improvement over the control group (CRT OFF) at six months.

Results: Patient quality of life (QOL) was assessed with the Minnesota Living with Heart Failure questionnaire. A lower score indicates an improvement in quality of life. Table 13 contains a summary of the improvement in Quality of Life in the two groups from baseline to 6 months.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± S (N = 83)
Baseline	42.0 ± 23	48.3 ± 24
6-months	45.4 ± 31	40.4 ± 22
Change	3.4 ± 31	-7.8 ± 22

Table 13. Improvement in Quality of Life Score (N=126)

The average improvement in the CRT ON group over the CRT OFF group was approximately 11 points. Objective met.

3. IMPROVEMENT IN SIX-MINUTE HALL WALK AT 6-MONTHS OVER BASELINE

Objective: To determine if the treatment group (CRT ON) shows an improvement over the control group (CRT OFF) at six months.

Results: Table 14 contains a summary of the improvement in 6-minute walk distance between baseline and 6 months.

	CRT OFF Mean ± SD (N = 43)	CRT ON Mean ± SD (N = 83)
Baseline	298 ± 94	284 ± 105
6-months	283 ± 150	297 ± 122
Change	-15 ± 142	13 ± 74

Table 14. Improvement in Six Minute Walk Distance (meters) (N=126)

The average improvement in the CRT ON group over the CRT OFF group was approximately 28 meters.

Additional Data

1. BIVENTRICULAR PACING AT 6-MONTHS

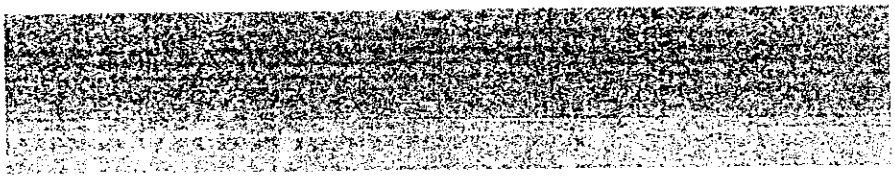
The average percentage of biventricular pacing at the 6-month visit in the 83 patients who were in the CRT ON group among the 126 patients in the primary resynchronization cohort was 95% ± 6%, with a range of 70% to 100%.

2. ECHO DATA

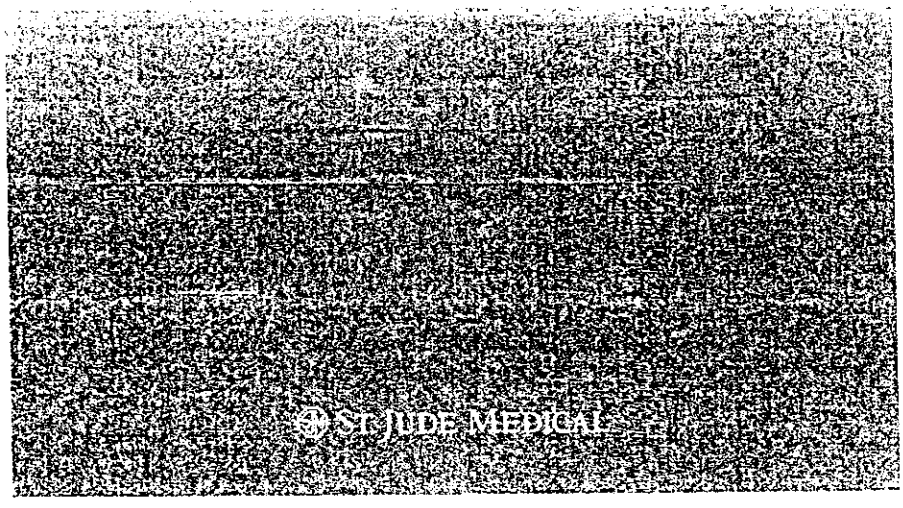
Echocardiographic analysis was performed at the baseline and 6-month follow-up visits. The following parameters were evaluated from the echocardiographic analysis: LVEDD, LVESD, LVEF, MR, E/A Wave Point Ratio, and Sphericity Index. Cardiac dyssynchrony (including Pre-Ejection Delay Time and Intraventricular Mechanical Delay) was also evaluated at baseline and 6-Months. Table 15 displays summaries of the improvement in these parameters between baseline and 6-months.

Parameter	CRT OFF (N = 40) Mean ± SD	CRT ON (N = 82) Mean ± SD
LVEDD (mm)	-2.4 ± 6.5	-4.3 ± 5.4
LVESD (mm)	-3.0 ± 6.4	-4.6 ± 7.0
LVEDV (ml)	-37 ± 53	-43 ± 69
LVESV (ml)	-36 ± 47	-43 ± 58
LVEF (%)	2.9 ± 6.2	4.3 ± 9.9
MR (grade)	0.10 ± 0.50	-0.06 ± 0.74
E/A Wave Point Ratio	-0.02 ± 1.2	-0.08 ± 0.8
Sphericity Index	0.02 ± 0.1	-0.02 ± 0.1
Pre-Ejection time (ms)	7.3 ± 33	-1.5 ± 52
IVMD (ms)	-6.4 ± 48	-14.5 ± 52
Tei Index	-0.05 ± 0.5	-0.4 ± 0.8
Contraction Interval (ms)	-55 ± 103	-94 ± 124

Table 15. Improvement in Echocardiography Parameters



A patient's Guide to Understanding
Cardiac Resynchronization Therapy Pacemaker (CRT-P)



Your Contact and Device Information

Have your doctor or nurse complete the information on this page before you go home from the hospital.

Physician Name_____

Phone Number_____

Address_____

_____

Hospital Name_____

Phone Number_____

Address_____

_____

Device Model Number_____

Serial Number_____

Date Implanted_____

Understanding Your Device

You have just received—or you're about to receive—a remarkable little device that can improve the quality of your life. It's called a *cardiac resynchronization therapy pacemaker*, but it's also known as a *"CRT-P"*. It helps to keep your heart pumping regularly and on time.

Invented in the 1950s, these amazing devices—about the size of a silver dollar—send small pulses of electricity to the heart to help it beat normally. The devices are run by tiny computer chips and sophisticated software. They are powered by batteries that last for years.

This booklet will answer many of your questions about your CRT-P. It will also tell you how the surgery is done and how to prepare for it. You'll also find out what happens after the operation, and how to avoid problems when you're living with your device.

A CRT-P is different from a standard pacemaker because two of its leads are implanted into the right and left ventricles. This means that the device can be used to stimulate both lower heart chambers to support the pumping of blood from the heart.

After reading this booklet, if you still have questions, discuss them with your doctor.

If you come across a word you do not understand, you can find its definition in the Glossary on page 44.

Table of Contents

The Healthy Heart

Why is the heart sometimes called a pump?

Your heart's job is to deliver oxygen and nutrients to all the organs and tissues of your body. Your heart does this by pumping blood from the lungs (where it picks up oxygen) to all the areas in your body (where it drops the oxygen off). The heart then pumps blood back to your lungs, completing the loop that keeps you alive day and night year after year.

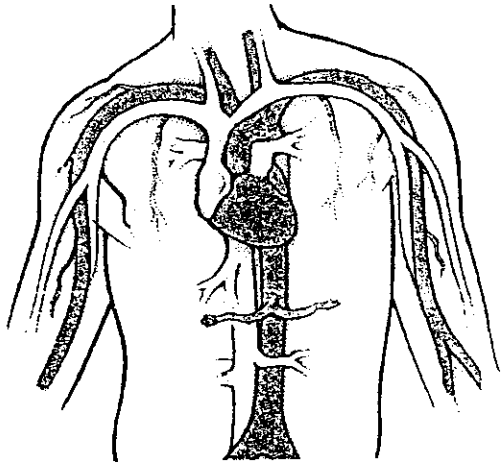


Figure 1. Blood flow through the heart.

What does the heart look like?

Your heart is divided into four connected *chambers*, each with a part to play in pumping blood. Oxygen-poor blood from the body enters the heart at the *right atrium*.

When the atrium is full, it pumps the blood into the chamber below it, the *right ventricle*. This larger chamber squeezes the blood out of the heart and into a blood vessel called the *pulmonary artery* that takes the blood to the lungs.

After picking up oxygen, the blood returns to the heart through the *pulmonary veins* into the *left atrium*. When the left atrium is full, it pumps the blood into the large chamber below it. The *left ventricle* then uses its strong muscles to pump blood into the body.

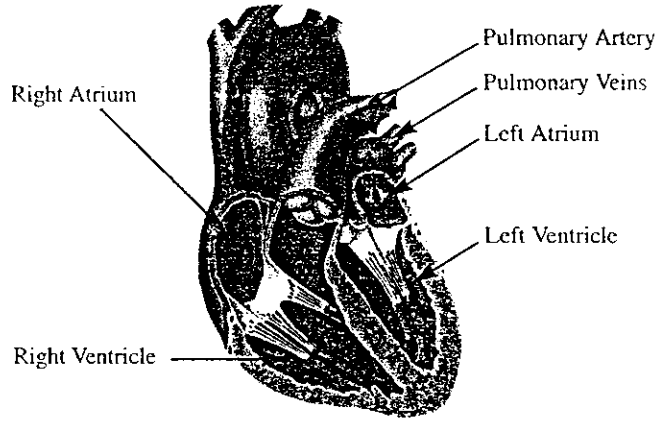


Figure 2. A typical heart.

How does the heart beat?

The millions of cells in your heart react to small *pulses* of electricity. Your heart

makes its own electrical pulses in a special area at the upper part of the heart called the *Sinoatrial Node* or *SA Node (see below).*

How often does the heart beat?

A normal heart beats 60 to 100 times each minute, regularly and in *rhythm*, so the time between each heartbeat is roughly the same. Depending on the body's need for oxygen, the heart can beat faster or slower. Your body tells your heart how much oxygen it needs.

What is the Sinoatrial (SA) Node?

The SA Node is a cluster of specialized cells in the atrium that produces tiny electrical signals and sends them to the rest of the heart.

The SA Node senses when the atrium fills with blood and sends out an electrical pulse that causes the muscles in the atrium to contract. This *contraction* pushes the blood in the atrium down into the ventricle.

What is the AV Node?

The *AV Node* or *Atrioventricular Node* is another specialized cell cluster, located between the atrium and the ventricle. It holds the pulse for just a few hundredths of a second before releasing it into the ventricle. The result is that the atrium beats first, pushing blood into the ventricle, and then the ventricle beats after it has been filled with the blood from the atrium.

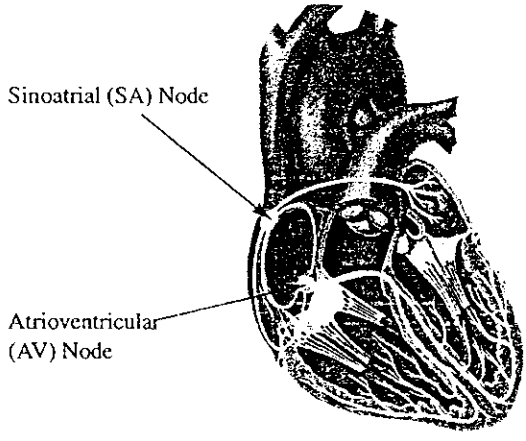


Figure 3. The Sinoatrial (SA) Node and Atrioventricular (AV) Node.

Arrhythmias

What is an arrhythmia?

An *arrhythmia* (pronounced "a-RITH-me-a") is any abnormal heart rhythm. It could be irregular, too fast, or too slow.

What causes an arrhythmia?

Many conditions and substances affect the heart's rhythm. Diseases like diabetes, hypertension, heart disease, chronic obstructive pulmonary disease, and hyperthyroidism can cause arrhythmias. Alcohol and certain drugs can cause arrhythmias, and so can drug withdrawal. Some people are born with hearts prone to arrhythmias. Some people have their heart's electrical system damaged by a heart attack or poisons. Even emotional swings, caffeine, and pregnancy affect the heart. Finding the cause of an arrhythmia is important because the treatment depends on the cause. Your doctor may order tests and procedures to diagnose the cause of your arrhythmia.

What are the different kinds of arrhythmia?

Too Slow—Bradycardia

Bradycardia means "slow heart." A heart that beats too slowly all the time can make a person tired, dizzy, or light-headed because a slow heart is not pumping enough blood to provide the body with as much oxygen as it needs. A *cardiac resynchronization ther-*

apy pacemaker (CRT-P) can be used to make a person's heart beat normally.

Too Fast—Tachycardia

Tachycardia means "fast heart." If the heart beats too fast all the time, its chambers may not fill completely with blood. The heart will not be able to pump enough oxygen to the body and the result will be dizziness, fainting, and even cardiac arrest. Some tachycardias occur in the top chambers of the heart and some occur in the lower portion.

Ventricular Fibrillation

This is the most serious kind of arrhythmia, where the heart's electrical signals aren't timed correctly and start in the ventricle instead of the SA Node. The result is that the heart "fibrillates" or quivers instead of beating regularly. A fibrillating heart pumps very little blood to the body, and a person in ventricular *fibrillation* quickly loses consciousness. Untreated ventricular fibrillation can be fatal.

To treat ventricular fibrillation, doctors use *de-fibrillation*, which is a large electrical shock to the heart that returns the heart to its normal rhythm. The shock can come from a machine with large paddles, or it can

come from an *ICD* (Implantable Cardio-verter-Defibrillator) implanted within the body.

Atrial Fibrillation

This is the most common arrhythmia in older people. In atrial fibrillation, the upper chambers of the heart are quivering (or "fibrillating") and the signals sent to the lower chambers are irregular and erratic. Some people may not feel any effects of atrial fibrillation. But in many people, this arrhythmia causes a feeling of pounding or fluttering in the chest. It may make people feel tired, sluggish, dizzy, or short of breath.

More serious is the fact that atrial fibrillation can cause a blood clot inside the heart that can flow to any part of the body, where it can cause a stroke or embolism.

Doctors can treat atrial fibrillation with a combination of surgery, medications, AV nodal ablation, and defibrillation.CRT-Ps can also be used to treat some patients with atrial fibrillation, depending on the cause and type of arrhythmia.

Asynchrony

Besides beating too fast or too slow, the heart can also beat irregularly. For example,

one side of the heart may contract sooner than the other side. When this happens, blood and oxygen are not delivered fast enough to the body and the pumping mechanism begins to fail. If blood is not pumped out of the lungs and the body, it backs up, causing congestion like a traffic jam.

This can lead to a serious condition called *congestive heart failure or heart failure.*

What is heart failure?

Besides beating too fast or too slow, the heart can also beat irregularly. In some patients, one side of the heart may contract sooner than the other side. When this happens, the pumping mechanism begins to fail. Blood and oxygen are not delivered fast enough to the body. This condition is called heart failure.

This condition is usually treated with drugs, but in some cases, a CRT-P can be used to help in the treatment. CRT-Ps can help the left and right ventricles beat at the same time (resynchronize the heart beat).

Some Basic Facts About CRT-Ps

What is a CRT-P?

CRT-P stands for cardiac resynchronization therapy pacemaker. It is a special type of implantable pulse generator to help resynchronize (coordinate) the lower heart chambers, enabling your heart to beat efficiently. A CRT-P can be used with your prescribed heart medications as part of your treatment plan.

To treat heart failure, the CRT-P monitors your heart signals and sends electrical pulses to the lower chambers of your heart and enables them to contract more efficiently.

These St. Jude Medical® CRT-Ps have three leads: one in the right atrium, one in the right ventricle and one in the left ventricle. These can help the left and right ventricle beat at the same time.

The CRT-Ps described above can also be *rate-modulated*. That means the CRT-P can speed up when the patient becomes more active and slow down when the patient is resting. Also known as "rate-responsive" or "rate-adaptive," this type of CRT-P has a sensor so it knows when the patient is moving. For example, a rate-modulated CRT-P will speed up when a person jogs. When the

person stops to rest, the CRT-P slows the heart rate.

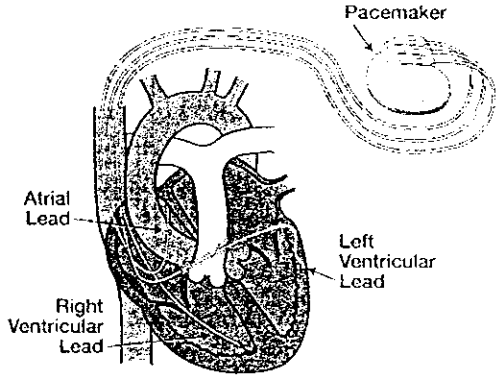


Figure 4. A CRT-P system.

Why do I need a CRT-P?

Your doctor has determined that despite taking medication for heart failure, you still have heart failure symptoms. In many cases, a CRT-P can help your heart beat properly. To treat heart failure, the CRT-P monitors your heart signals and sends electrical pulses to the lower chambers of your heart and enables them to contract more efficiently.

Implantation of a St. Jude Medical CRT-P is indicated for:

- Maintaining synchrony of the left and right ventricles in patients who have undergone an AV nodal

ablation for chronic atrial fibrillation and have NYHA Class II or III heart failure.

- The reduction of the symptoms of moderate to severe heart failure (NYHA Class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy (as defined in the clinical trials section), and have a left ventricular ejection fraction ≤35% and a prolonged QRS duration.
- Patients who have undergone an AV nodal ablation for chronic atrial fibrillation or have heart failure.

Who does not need a CRT-P?

If your conditions are reversible, temporary, or can be controlled solely by drugs or other methods, you do not need a CRT-P. If you are not taking medication for heart failure you should not receive a CRT-P. There is more about medication in a later section of this booklet.

What does a CRT-P do?

The CRT-P can sense the heart's rhythm. CRT-Ps can be "programmed" to either send out a pulse or to wait for the heart to beat on its own. Some CRT-Ps also sense the patient's activity — for example, climbing stairs or exercising — so that it can speed up or slow down the heart rate.

After a CRT-P is inside the body, its settings can still be changed. Doctors and clinicians "talk" to it with a *programmer*. This is a computer with a wand that sends signals through the body to the CRT-P. The procedure is painless. The programmer also displays information the CRT-P has collected about the heart.

What does a pulse feel like?

Most people can't feel it at all. The electrical pulse of a CRT-P is very small. If you do feel a pulse, your doctor or clinician may change the settings to make you more comfortable.

What happens when the battery runs down?

A CRT-P lasts, on average, five to ten years. How long it lasts depends on the type of battery, how often it sends a pulse, the patient's medical condition, and other factors.

The battery does not suddenly stop working. It gradually runs down over a period of months, usually with more than enough time to schedule a replacement. Doctors and clinicians check the battery at each follow-up visit. When the battery energy gets low, the CRT-P has to be replaced with a new one, and you must have another operation.

What happens if your lead needs to be replaced?

If your lead needs to be replaced, surgery is required to replace it.

Risks and Benefits

CRT-Ps are not a cure for heart disease. They don't treat the causes of slow or irregular heartbeats. But because they can keep the heart pumping for years, CRT-Ps can greatly improve the quality of life for people with arrhythmias.

What are the benefits of having a CRT-P?

A CRT-P improves the ability of the heart to pump regularly and on time. Some people must rely completely on the CRT-P to make the heart beat.

Many patients get relief from symptoms such as light-headedness, dizziness, and fainting. Some people feel they have more energy.

A CRT-P also gives many patients "peace of mind." They feel safer because the CRT-P can keep their hearts beating.

A CRT-P may also help alleviate your heart failure symptoms, such as fatigue or shortness of breath. You may experience other benefits from a CRT-P. Your doctor is the best person to help you understand them.

What are the risks of having a CRT-P?

A small number of patients develop complications from the operation to implant the CRT-P and the leads in the body. These can include infection, a reaction to a drug used

during surgery, blood loss, or damage to a blood vessel, the heart wall, or other organ. These complications can usually be corrected or cured.

The CRT-P may not always eliminate all symptoms of the arrhythmia. You still may feel lightheaded or dizzy, or you may faint.

After the surgery, you may feel some discomfort or feel tired, but these feelings only last a short time. Some patients, however, may continue to feel a bit uncomfortable in the area where the CRT-P was implanted.

Modern CRT-Ps have many safety features. Sometimes, a CRT-P may not act properly because it is being affected by outside sources of electromagnetic energy. (This is discussed on page 27.)

It is also possible for the tip of the lead to shift in the heart so that the pulse is no longer effective. Very rarely, the device may slip out of the "pocket" in the chest. (See the section on surgery below.)

Finally, remember these are man-made devices. It is important to monitor the device regularly with follow-up visits as often as your doctor recommends.

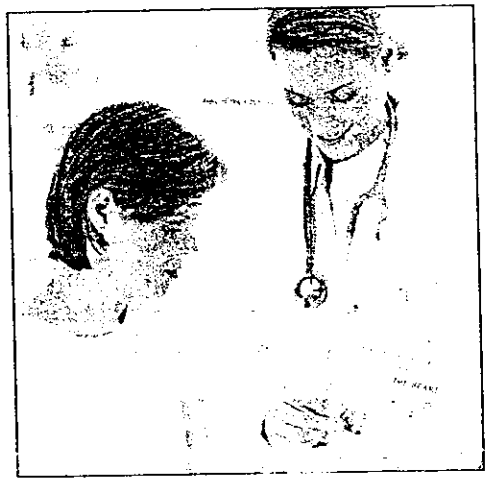
Contact your doctor if:

- You notice you are tired, short of breath or your heart rate is changing.
- Symptoms you had before the CRT-P was implanted seem to return.

Surgery for the CRT-P System

What will the operation be like?

Surgery to implant a CRT-P is routine. In many cases, the operation takes one to two hours, and patients may go home the same day.



However, each patient is unique, and the surgery will differ from person to person.

The following sections discuss what generally happens to patients during a CRT-P operation. Your doctor will give you details about what will happen during your own surgery.

What happens before the operation?

Before the surgery, your doctor will tell you how to prepare for the operation. You may have to stop taking one or more of your medications beforehand. Usually, patients are asked not to drink or eat for several hours before the operation. A technician may take a blood sample. Some doctors will also ask patients to complete insurance and other forms.

What happens on the day of the operation?

You will be taken to an operating room where a nurse or clinician will shave and wash your upper chest or abdomen. You may have an IV (*intravenous*) line placed in your arm and a blood pressure cuff around your arm. ECG (*electrocardiogram*) electrodes will be placed on various parts of your body.

Most patients stay awake for the procedure, and receive a shot of a *local anesthetic* to numb the area where the CRT-P will be placed. If you are going to be given *general anesthetic*, an anesthesiologist will give you medications to put you to sleep.

What happens during the surgery?

After the skin of the shoulder or chest is cleaned and numbed with an anesthetic, the doctor makes a cut through the skin about one to two inches long. The doctor then finds a vein and threads the leads directly into the heart, using a fluoroscope to see where it will go. You should not feel the leads in your heart.

The doctor then makes a small "pocket" under the skin. The doctor fits the CRT-P into the pocket and connects it to the leads. The CRT-P is then tested to make sure it is working properly.

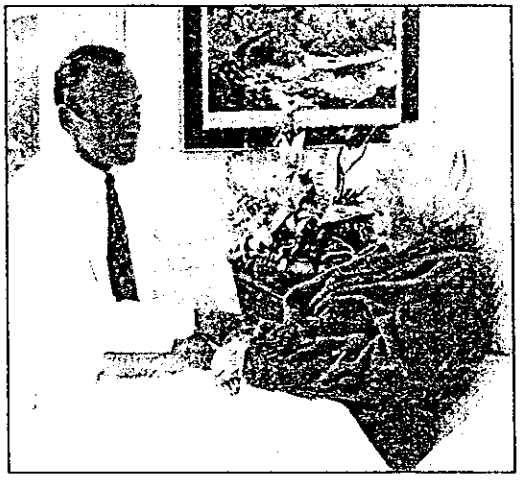
You may feel some pressure while the CRT-P and leads are being inserted. If you begin to feel increased discomfort, let the doctor know immediately.

What happens after surgery?

You will be taken to a recovery room where nurses will look after you to make sure you are doing well. You may feel some soreness

where the CRT-P was implanted. You will be given pain medication if you need it.

Later on, the doctor or clinician will test your CRT-P to make sure it is working properly.



Many patients go home the same day. Other patients may need longer to recover and will stay overnight before going home.

Coming Home After Surgery

What will happen when I get home from the hospital?

For the first few days or weeks after your operation, you will need to recover. The wound should gradually heal. You should feel better. At first, you may be aware of the CRT-P, but after a while you will become accustomed to it.

Right after the operation, you should:

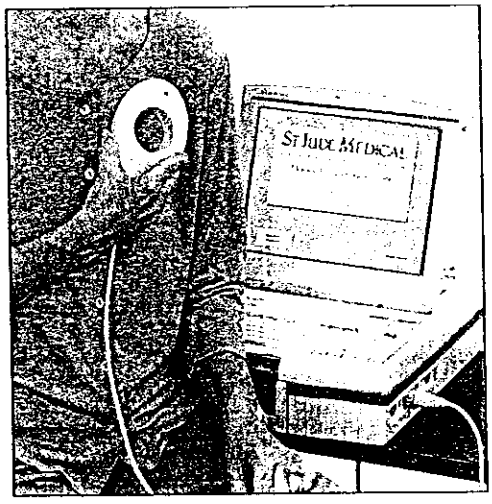
- Keep the wound clean and dry. If you notice that the wound is red, hot, swollen, more painful or starts to drain fluid, call your doctor immediately.

- Follow the instructions about bathing, changing the wound dressing and resuming activities.
- Use only gentle movements with the arm closest to the CRT-P. Avoid stretching, lifting, and sudden, jerky movements. As you heal, gradually increase the use of your arm.
- Do not play with or move the CRT-P under your skin. Try not to hit it or bump into it.
- Keep your doctor appointments.
- Keep your Patient Identification Card with you at all times.
- If your symptoms do not improve, call your doctor. Do not wait for a follow-up visit.

What happens at follow-up visit?

A follow-up visit normally takes place in a doctor's office or in a clinic. The visit is painless. After a brief physical examination, the clinician or doctor usually attaches ECG electrodes to your chest. They will then place the wand over your chest and use the *programmer* (the computer that talks to the CRT-P) to display and print out information about your heart and the CRT-P. With this information, the doctor can check the settings on the CRT-P. If any changes

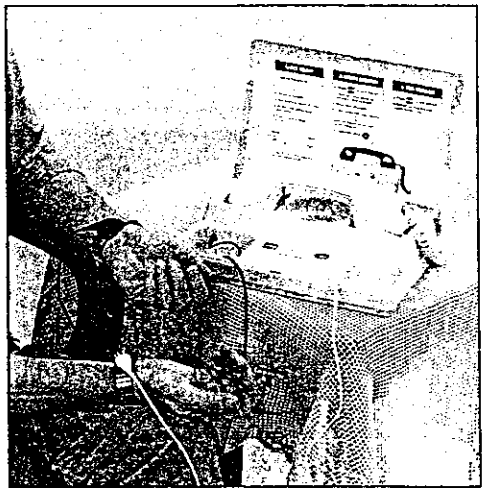
are needed, they can be done right away. They will also check your CRT-P's battery.



Be sure to tell your doctor or clinician about any problems you may be having with the CRT-P, your heart or your health in general. It's also a good time to ask questions about your CRT-P.

What is remote monitoring?

Remote monitoring is the use of a telephone or computer to send information to the doctor about your CRT-P. Some doctors ask patients to "phone in" information instead of coming in for a follow-up visit. Many doctors use remote monitoring along with visits to the clinic.



There are a number of different systems for remote monitoring. They are all fairly easy to use. Some are held over the CRT-P and then held over the phone. Some use computers and modems to send in the information. Your doctor will give you instructions on how to use phone monitoring.

When can I get back to my old life?

Each person's recovery period is different, but eventually, you may be able to return to your normal life with very few changes.

Your wound should be completely healed before you return to your usual daily activities. Talk to your doctor about how soon you can return to work, drive your car, begin exercising, or go away on a trip.

Living with Your CRT-P System

What is a Patient Identification Card?

This card lets everyone know that you have a CRT-P. It contains information on the type of CRT-P you have and other important information. If you're ever in a medical emergency, this card will give emergency personnel critical data that could save your life. Keep it with you at all times.

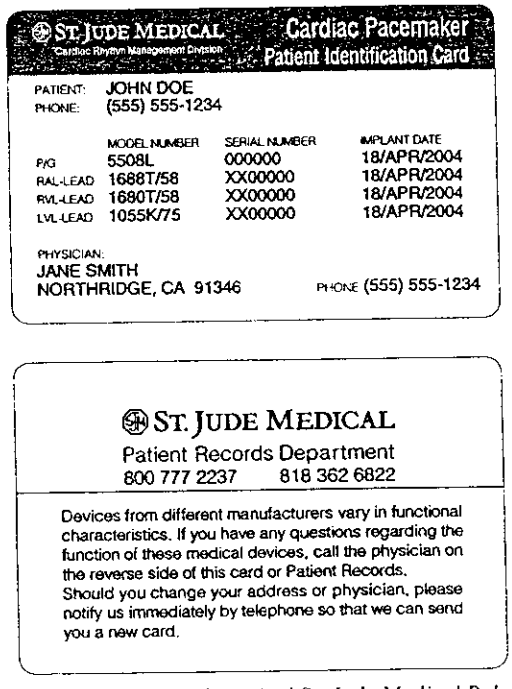


Figure 5. Example of a typical St. Jude Medical Pulse Patient Identification Card.

Will a CRT-P limit the things I do?

One of the reasons for getting a CRT-P is to help you lead a fuller life. At home, most people will have no restrictions on their activity. If you work with heavy electrical equipment that causes *EMI*, tell your doctor.

Precautions and Warnings

What is EMI?

EMI means *electromagnetic interference*. Certain types of electrical or magnetic energy can interfere with your CRT-P's operation. You should do your best to avoid some major causes of EMI, explained below.

What causes EMI?

EMI or electromagnetic interference can be caused by:

- Electrical appliances in poor condition or not grounded correctly
- Electrical equipment that produces a great deal of energy, like industrial generators

- High-voltage transmission lines and equipment, arc or resistance welders, induction furnaces.
- Communication equipment, such as microwave transmitters, linear power amplifiers, or high-power amateur transmitters.
- Metal detectors and security systems used in stores and airports.
- Magnetic resonance imaging (MRI) scans, which can severely damage your device when you are in or near an MRI room.
- Transcutaneous Electrical Nerve Stimulation (TENS) units, which are electrical nerve and muscle stimulators.
- Therapeutic radiation, such as cancer radiation therapy.
- Electrosurgical cautery, which can inhibit the operation of your device.

What should I do if I am near a source of EMI?

In most cases, you can just walk away from the EMI source or turn it off. At airports, show the security personnel your Patient Identification Card so that you do not have to walk through the metal detector.

If you feel symptoms after being near an EMI source, contact your doctor.

What electrical equipment is safe to use?

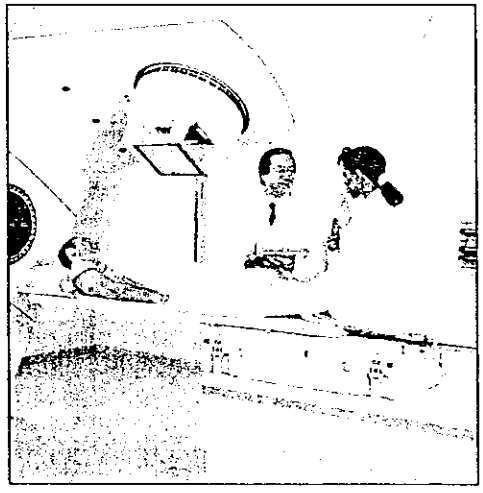
Most home appliances in good working order and properly grounded are safe to use. This includes microwave ovens, blenders, toasters, electric knives, televisions, VCRs, electric blankets, stoves and garage door openers.

Office equipment and most medical equipment is also safe to use. The CRT-P will work properly during chest and dental x-rays, diagnostic ultrasound, CT scan, mammography, and fluoroscopy.

What if I am going into a hospital or clinic?

Tell the hospital personnel that you have a CRT-P before you undergo any medical or dental procedure or test.

Do not enter areas that have a "no pacer" symbol posted.



Talk to your doctor if you have to undergo the following medical procedures:

- Electrosurgery
- Electrocautery
- Lithotripsy
- Radiation therapy.

Do not undergo any diathermy procedure, even if your CRT-P has been turned off. It could cause damage to the tissue around the implanted electrodes, or permanent damage to the CRT-P.

External defibrillator paddles should not be placed directly on your device or leads. Carry your Patient Identification Card at all times so emergency personnel are aware of your device if necessary.

Will a cellular phone interfere with my CRT-P?

You can use a cellular phone without any problems with St. Jude Medical cardiac resynchronization therapy systems. Contact St. Jude Medical for more information about using a cellular phone.

What about security systems?

Security systems, like the ones used at entrances, exits, or checkout counters are also sources of EMI. When you enter or leave a place with security system, walk through the entrance or exit at a normal pace. Do not linger in these areas.

Are there any precautions I need to take at home?

It is safest to live in a home that has a properly grounded electrical system, so three-prong plugs fit right into the wall. Poor grounding can cause EMI. An evaluation of wiring by an electrician, particularly in older homes, would identify any improper grounding.

Keep your tools and appliances in good running order. Don't use products with breaks in the power cords. If you're fixing your car, remember that your car's electrical system (alternators, high-tension ignition wires, spark plugs, and coil wires) can be a source of EMI.

Some stereo speakers contain large magnets which can interfere with CRT-P.

Electric razors, vibrators, or handtools held directly over the CRT-P may affect its operation. Some CRT-Ps respond to pressure, so your doctor may tell you to avoid sleeping on the CRT-P.

Do not manipulate your implanted CRT-P since it may result in lead damage or lead displacement.

What precautions should I take at work?

If you work near large sources of EMI (see list above), you should discuss this with your doctor and employer. You may be able to limit your exposure to these sources.

Magnets, large heaters, and radio transmitters can also cause EMI.

Work that involves severe shaking or physical contact should also be avoided.

Learning to Live with Heart Disease

My illness has changed my life. How do I cope with it?

Serious heart disease is a blow that can affect your emotions as well as your body. At times you may feel anxious, afraid, depressed, even angry. There are many ways to cope:

- Talk to other people. It will help you work through your feelings. Talk to your doctor, a nurse, a counselor, a friend or family member, or a member of the clergy.
- Talk to your doctor about joining a support group. Sharing experiences with other CRT-P patients lets you know that you are not alone.
- Exercise regularly. It's a great way to reduce stress, build strength and gain confidence. Remember to ask your doctor before starting an exercise program. There is more about exercise later in this guide.
- Learn more about relaxation. Too much stress can wear you down

and increase your chance of getting other illnesses. It also disturbs your sleep and makes you cranky.

One good way to relax is to sit quietly with your eyes closed for 20 to 30 minutes twice a day. A short nap each day or a slow walk every morning can also be calming.

- Take care of yourself. Avoid alcohol and caffeine. And quit smoking. These habits can make anxiety and depression worse.

My spouse/family member is the patient. How can I help?

If a family member or friend is the patient, it is natural for you to have the same fears and worries. There are several things that can help both of you cope with their condition. For example, listen when they want to talk. Your loved one needs reassurance that they have your support. However, you should not deny that their illness is serious.

Drugs

Why do I need medication if I have a CRT-P?

Anti-arrhythmia drugs and the CRT-P can work together to improve the efficiency of your heart.

In addition to your CRT-P, you will also need to take medication as part of your heart failure treatment plan.

Warning: Do not stop taking your drug(s) without the advice of your doctor!

I'm told that my drugs may need periodic adjustments. How will that be done?

Your doctor may find it necessary to increase or decrease your drug dosage. They may also add a new drug. Your heart must be watched closely while your doctor makes these changes. This means that you may need to stay in the hospital. The length of the hospital stay varies from patient to patient.

Is it OK to take my anti-arrhythmia and heart failure drugs with other drugs?

Make sure your doctor knows about all of the drugs you are currently taking. Tell your doctor whenever another doctor prescribes a new drug.

Food and Nutrition

I already have heart disease. Will changing my diet benefit me?

It is never too late to improve your diet. The American Heart Association recommends a diet high in fiber and low in fat, cholesterol and sodium (salt). High-fat, high-cholesterol foods (such as whole milk dairy products, red meats and junk foods) contribute to hardening of the arteries—a major cause of heart attacks and strokes. High-fiber foods are rich in vitamins and minerals and make you feel full and satisfied for fewer calories.

What are good sources of fiber?

Oatmeal, fresh vegetables, and fruit are good sources of fiber. Fiber helps lower blood cholesterol and prevents constipation.

How much fat can I have?

Generally, you should keep saturated fat to less than one third of your daily fat intake—10% of daily calories. A fat-rich diet raises blood cholesterol and can lead to weight gain, both of which contribute to heart disease. Most packaged foods list fat, cholesterol and fiber content on their labels. Talk with your doctor about your

specific dietary requirements and changes you may need to make in your eating habits. A registered dietitian is a wonderful resource to help you learn more about eating to be "heart healthy."

What is the best way to control my fat intake?

Let balance, variety and moderation guide you. There is no need to give up meats and dairy products. Eat lean cuts of meat and low-fat dairy items. Save high-fat foods such as potato chips and cheesecake for special occasions.

Avoid saturated fats. These are found mostly in red meats, whole milk products, and foods made with palm and coconut oil. In general, saturated fats come from animals.

Sometimes it is not obvious that a food is high in fat. For example, one ounce of trail mix with peanuts and raisins has as much fat as one chocolate chip cookie.

What foods are high in sodium?

Salty foods and those foods with preservatives generally have a high sodium content. For example, broth, soy sauce, cold cuts, hot dogs, chips, nuts and pretzels are high in sodium. Sodium may encourage high blood pressure and water retention. Reducing the sodium in your diet is simple if you take note of the food products

labeled as "low sodium." Ask your doctor how much sodium is OK for you.

Besides diet, what affects heart health?

Many factors contribute to heart disease. Some things you can't change, like your sex, race, age, high blood pressure and family. You can change other things that affect your heart, like smoking, a poor diet and lack of exercise. If you have high blood pressure, have it checked regularly and follow your doctor's instructions to keep it under control.

Why is being overweight dangerous for a person with heart disease?

When you're overweight, the extra pounds make your heart work harder. They can also lead to high blood pressure and diabetes, which are bad for the heart. Losing excess weight eases the strain on your heart.

If you diet, you should lose weight slowly, ideally one-half to one pound a week. You will be more likely to keep the weight off. Your doctor can help you set up a weight-loss program.

Exercise

What kind of exercise can I do after surgery?

After surgery you should resume your normal activity as soon as you feel up to it. You may feel a little tired or sore at first, so build slowly up to your normal routine. Before long, you'll feel more like yourself. Your doctor may give you special exercise instructions or suggest that you start a cardiac rehabilitation program.

In most cases, your CRT-P will not limit your fun. There are only a few exercise restrictions to keep in mind. Avoid rough contact sports that might damage your CRT-P—like wrestling, football, soccer or rugby—since they may damage the CRT-P or the leads. Consult your doctor before doing strenuous or repetitive upper-body exercise like weight lifting or softball.

It's also best to avoid activities that involve severe shaking, like horseback riding or bumper cars. Depending on the programming of your device, this type of activity may inappropriately cause a temporary increase in the rate of pacing.

Strenuous or repetitive upper-body exercise, like weight lifting or softball, can in some cases affect your CRT-P or leads.

Before you begin any vigorous exercise or activity, talk to your doctor.

Warning: Avoid contact sports after you get your CRT-P. Also, get your doctor's approval before starting an exercise program, especially if it involves upper-body activity.

No matter what kind of exercise you do, be sure to wear loose clothing and comfortable walking shoes. Feeling comfortable will help you get the most benefit and enjoyment from exercising.

What is cardiac rehabilitation?

It is an exercise and education program to help you regain your strength and

improve your heart. A typical program consists of regular exercise monitored by medical professionals. Walking and bicycling are the most common exercises. You will also attend classes to learn more about your heart, the reasons for your heart disease, and how to live a healthier life.

Ask your doctor if this kind of program would be good for you. They will develop one specifically for you.

Other Questions?

If you have any other questions or would like more information about your CRT-P, call Technical Services at the phone numbers below.

In North America:

1-818-362-6822

1-800-722-3774
(toll-free in North America)

1-818-362-7182 (FAX)

Glossary

Anesthetic	A substance that produces numbness or sleep.
Arrhythmia	An abnormal rhythm of the heart.
Atrioventricular (AV) Node	The small mass of special tissue that delays the energy pulse traveling from the SA Node to the lower chambers (ventricles) of the heart.
Atrial	Relating to the atrium.
Atrium	One of the two upper chambers of the heart, the right atrium and the left atrium. These chambers receive blood from the body and pump it to the ventricles, the lower chambers of the heart. (Plural = *Atria*)
Bradycardia	An abnormally slow heart rate.
Cardiac Resynchronization Therapy Pacemaker (CRT-P)	A system comprising a device and three leads: one in the right atrium, one in the right ventricle and one in the left ventricle. These can help the left and right ventricle beat at the same time.
Chamber	One of the four areas in the heart that fill with blood before contracting during the heartbeat. The four chambers are: right

	atrium, left atrium, right ventricle, and left ventricle.
Congestive Heart Failure	The failure of the heart to pump enough blood to the rest of body, resulting in congestion of blood in the lungs and tissues.
Contraction	Heartbeat. A squeezing of the heart muscle that forces blood out of the heart.
Defibrillation	The use of electric shock to correct rapid heartbeats, usually tachycardia or fibrillation. Defibrillators can be paddles on the outside of the chest or small internal electrodes placed directly on the heart.
Electrocardiogram	Often called an EKG or ECG, it is a recording of the electrical activity of the heart.
Electromagnetic Interference	Also known as EMI, this is magnetic or electrical interference from machines or devices which can interrupt the normal operation of a CRT-P.
Electrophysiologist	A doctor who specializes in diseases of the electrical system of the heart.
EMI	See "Electromagnetic Interference."

Fibrillation	An arrhythmia in which the heart quivers rapidly. Atrial fibrillation occurs in the atrium and is usually not life-threatening. Ventricular fibrillation occurs in the ventricles and can be fatal.
General Anesthetic	A medication or group of medications that will make the patient unconscious during surgery.
Heart Failure	Heart failure (HF) is a complex clinical syndrome that results when the heart muscle is weakened and can no longer pump blood as efficiently as a healthy heart.
ICD	Implantable Cardioverter-Defibrillator; an implanted pulse generator used to treat ventricular fibrillation and tachycardia by delivering electrical shocks directly to the heart.
Intravenous (IV)	Inside a vein.
Lead	A special wire connected to the CRT-P and placed inside the heart.
Local Anesthetic	A medication used in surgery that numbs only one area of the body while the patient stays awake.

Node	A cluster or a place where things join, for example, the Sinoatrial Node is where many nerves join.
Pacemaker	Another term for *pulse generator.*
Programmer	A special computer designed to communicate with or "program" an implanted CRT-P.
Pulmonary Artery	A blood vessel that carries blood from the right ventricle to the lungs.
Pulmonary Vein	A blood vessel that carries blood from the lungs to the left atrium.
Pulse	A short burst of electricity.
Pulse Generator	A sealed device containing electronic circuitry and a battery, that is designed to send out electrical pulses and correct problems with the heart's rhythm.
Rate-Modulated	A CRT-P that can sense a person's activity and change the heart rate accordingly.
Remote Monitoring	Using a device or machine to transmit information about your CRT-P over a phone line.
Rhythm	The regular beating of your heart.

Sinoatrial (SA) Node	The small mass of special tissue that generates a heartbeat. It is located in the upper right chamber of the heart.
Tachycardia	An abnormally fast heart rate.
Ventricle	The two lower chambers of the heart. These chambers pump the blood out of the heart into the body.
Ventricular	Relating to the ventricle.

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Notes

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